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THE RESISTANCE (OR IMMUNITY) DEVELOPED BY THE REACTION TO SYPHILITIC INFECTION

AND SOME OF THE EFFECTS OF THE SUPPRESSION OF THIS REACTION *

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The idea of an inhibitory influence has been suggested as a means of explaining certain phenomena of syphilitic infections and there is some experimental evidence on which to base such a conception. The difficulty has been that most of the evidence cited in support of this theory was susceptible of more than one interpretation. This applies in particular to reinoculation and superinfection experiments which have been the favorite means of demonstrating inhibitory effects. Nowhere, however, is the action of such an influence more strongly suggested than in the experimental infection produced in the rabbit by scrotal or testicular inoculations of well adapted strains of *Spirochaeta pallida*.

As it is ordinarily seen, the two most striking features of this infection are an extremely marked reaction at the site of inoculation and a total absence of generalized manifestations of disease. If one considers these peculiarities of the experimental infection as compared with that in man, one can hardly fail to see a possible connection between the two conditions mentioned, especially when it has been shown that the absence of generalized lesions in the rabbit cannot be accounted for either by a lack of dissemination of spirochetes or by a tissue insusceptibility.

It appeared to us that the reaction to infection as it occurred in the rabbit offered an opportunity for determining the influence which a syphilitic reaction in one part of the body might exert on manifestations of the disease elsewhere and, at the same time, a possibility of modifying the experimental infection so as to increase its usefulness as a means of investigating problems of human syphilis.

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Accordingly, a series of experiments was carried out with a view to determining the effect which a simple reduction or suppression of the reaction at the site of inoculation might have on other clinical manifestations of the infection.

EXPERIMENTAL

The means employed in making these comparisons were unilateral as contrasted with bilateral inoculation, unilateral and bilateral castration at various stages of the infection, suppression of the primary reaction by the use of therapeutic agents and complete prevention of a primary reaction. (Castrations were made under ether anesthesia.)

The effects produced were gaged on the basis of the occurrence of generalized lesions. In the rabbit, the conditions which one may recognize clinically include various forms of cutaneous lesions, lesions of the mucous membranes, lesions of the periosteum and bones, lesions of the eyes and a general lymphadenitis. The latter condition is of such common occurrence, even when no other clinical sign of generalized infection can be recognized, that it was not used as a standard of comparison.

The results obtained from these experiments will not be reported in detail, but the essential character of the effects produced by the procedures indicated will be given briefly.

EFFECTS OF UNILATERAL AND BILATERAL INOCULATION AND OF CASTRATION

In the first group of experiments, a comparison was made of the effects of unilateral and bilateral inoculation and of the removal of the infected testicles soon after the appearance of the initial lesions. The results of these procedures were determined on the basis of a period of four months' observation.

Bilateral Inoculations.—Of twenty rabbits inoculated in both testicles, fourteen were castrated and six were held as controls. Generalized lesions developed in one of the six controls and in thirteen of the fourteen castrated animals within the period of observation.

Unilateral Inoculations.—Twenty-seven rabbits were inoculated in one testicle only; fourteen of these were castrated and thirteen were held as controls. In this series, generalized lesions developed in eight of the thirteen controls as contrasted with one of six animals inoculated in both testicles and again in thirteen of the fourteen castrated animals.

Several other experiments of a similar character gave essentially the same results, thus showing that by inoculating one testicle instead of two, the incidence of generalized lesions was markedly increased.

When the reaction at the site of inoculation was further reduced by early removal of the infected organs, generalized lesions developed in almost every instance.

EFFECTS OF SUPPRESSION OF PRIMARY LESIONS BY THERAPEUTIC AGENTS

In a second set of experiments in which castrations were made at different stages of the infection, the effects of suppression of the testicular lesion by the use of a therapeutic agent was also tested. For this purpose, a drug was chosen from among those studied by us in collaboration with Dr. W. A. Jacobs and Dr. Michael Heidelberger, whose effect in inducing resolution of syphilitic lesions was much greater than its spirocheticidal action. This substance was arsenophenylglycyl dichloro-m-aminophenol.

Twelve rabbits, six of them inoculated unilaterally and six bilaterally, were given a single intravenous injection of this drug (5 mg. per kilo) fourteen days after inoculation, and the results were controlled by six untreated rabbits from each of the respective groups.

In the unilateral series, the lesions present were almost completely resolved and the local reaction suppressed for between two and three weeks. At the end of three months, all of these animals had developed generalized lesions as contrasted with three of the six controls. The effect of the drug on the animals inoculated in both testicles was less marked and lasted for only from seven to ten days. At the end of three months, generalized lesions had developed in four of the six treated animals and in one of five surviving controls.

This experiment showed that by properly gaging the dose of a therapeutic agent so as to suppress the lesions present without destroying the infecting organisms, the infection can be intensified in the same way as by an excision of the primary lesions.

EFFECTS OF COMPLETE PREVENTION OF A REACTION AT THE SITE OF INOCULATION

In another experiment, the reduction of the reaction at the site of inoculation was carried to the point of complete prevention. This was accomplished by inoculating ten rabbits in the right scrotum, using tissue implants, and at the end of forty-eight hours completely excising the scrotum and testicle of that side under ether anesthesia.

By the end of the seventh week, eight of the ten rabbits in this series showed a marked generalized syphilis and the other two developed slight generalized lesions at the end of two and two and one-half months.

Taken as a whole, the generalized infection in this series of animals was the most pronounced which we have seen in any single group

of rabbits. This would indicate that both the incidence and severity of the generalized infection tend to increase in proportion to the reduction or suppression of the reaction at the site of inoculation.

CONCLUSION

These experiments show that, in so far as syphilitic infections in the rabbit are concerned, the reaction which takes place at the site of inoculation tends to dominate the entire course of the infection; that, in effect, this reaction either inhibits or obviates the necessity for the development of lesions elsewhere and, conversely, that the reduction or suppression of the reaction by the use of any means that does not exercise an equal effect on the organisms themselves, removes this control and tends to increase the occurrence of generalized lesions and the severity of the infection.

If one is prepared to accept the infection produced in the rabbit by *Spirochaeta pallida* and the reaction to infection on the part of the experimental animal as analogous in kind to those in man, these observations become of far reaching importance and may open the way to a better understanding of many problems of human syphilis.

PROVOCATIVE REACTIONS IN THE CEREBROSPINAL FLUID IN NEUROSYPHILIS *

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The provocative arsphenamin reaction in the blood is a familiar phenomenon. In many clinics, when a patient suspected of having syphilis gives a negative Wassermann reaction, an injection of arsphenamin is given; then the blood is tested at daily intervals thereafter, because it apparently has been shown that after the injection of arsphenamin the Wassermann reaction will be positive in some cases.

It is our purpose to call attention to a similar reaction taking place in the spinal fluid. We report several cases in which, after either intravenous or intraspinal injections, a negative spinal fluid became positive, or the positive pathologic findings were intensified. From the clinical standpoint, the phenomenon of intensification of symptoms relating to the central nervous system has frequently been described as occurring after treatment. To this phenomenon the term neurorecidive or neurorecurrence has been applied. One is not sure in these cases whether the resulting intensification of symptoms is due to the introduction of the drug or whether it is a mere coincidence that an increase of symptoms appears following the injection. However, in relation to secondary syphilis, the intensification of symptoms following arsphenamin injection has occurred so frequently that it has been considered as due to liberation of toxins resulting from the lytic action of arsphenamin on the spirochetes. This is the so-called Herxheimer reaction. If this can occur in skin lesions, there is every

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reason to suppose, a priori, that the same thing may occur in neurosyphilis. However this may be, the following cases would appear to show that following intravenous and intraspinal injections of arsphenamin or arsphenamized serum, the spinal fluid findings may become more strongly positive.

REPORT OF CASES

CASE 1.—*History.*—F. H., aged 36, according to the history obtained from the patient, had experienced a sudden paralysis of the right leg and arm about eighteen months previous to his admittance to the clinic. He recovered from this in about two days. At the time his physician gave him a liquid medicine (potassium iodid?). During the three months preceding his admittance to the clinic he had been receiving intramuscular injections of mercury. He denied syphilitic infection, but admitted exposure. He also admitted excessive use of alcohol. He had been married five years. His wife was living and well, but had never been pregnant. At the time of admittance he complained of headaches, some loss of memory and a mild speech defect at times. The visceral examination revealed nothing abnormal.

Examination.—Neurologic: The pupils were equal and reacted to light. The left patella and biceps reflexes were more active than the right. Abdominal and cremasteric reflexes were normal. There were no abnormal reflexes. Muscle strength in the legs and arms was good. Station and gait were normal. Ophthalmoscopic examination showed a few vitreous opacities, but the disk and choroid were normal.

Mentally he seemed somewhat euphoric, boasting with great confidence of his abilities. No definite memory disorder or speech defect was noted.

The Wassermann reaction was negative on the blood and spinal fluid; the other spinal fluid tests, including cell count, globulin, albumin, and colloidal gold reaction, were negative.

There was a difference of opinion as to the diagnosis, some members of the staff diagnosing the case as neurosyphilis despite the negative laboratory findings. Because of this difference of opinion, the patient was given a provocative injection of arsphenamin. The blood was drawn at intervals of twenty-four, forty-eight and seventy-two hours after the injection; all tests were reported as negative. The spinal fluid was drawn some time later and gave the following reactions: Wassermann reaction positive with 1 c.c. and 0.8 c.c.; negative with 0.6 c.c. and with the higher dilutions. There were 53 cells per cubic millimeter; globulin was present; and albumin was present in excess. The colloidal gold reading was 244333000.

We may assume then, that a provocative reaction in the spinal fluid occurred as a result of the intravenous injection of arsphenamin, the reactions which had previously been negative becoming positive. This provocative reaction did not appear in the blood.

Blood and Spinal Fluid Reactions.—The following reactions were obtained before treatment: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, negative; globulin, 0; albumin, normal; cells, 0 per cubic millimeter; colloidal gold test, negative. After one intravenous injection of arsphenamin was given the reactions obtained were: Wasser-

mann reaction of the blood, negative; Wassermann reaction of the spinal fluid, 55 — — — — (positive);[1] globulin, 2; albumin, 2; cells, 53 per cubic millimeter; colloidal gold curve, 2443330000.

CASE 2.—*History.*—This patient came under observation in the routine follow-up of the families of our known syphilitic patients. His wife was suffering from general paresis. Both denied any history of infection, although some years before a stillbirth had led to a diagnosis of syphilis, and a small amount of treatment had been given to both husband and wife.

Examination.—When examined the patient was in good health, and the only significant symptom was an inequality of the pupils. The Wassermann reaction of the blood was negative, but in view of the inequality of the pupils, a lumbar puncture was performed. This showed a Wassermann reaction positive with 1 c.c. of fluid, but negative with the higher dilutions. Globulin was absent; albumin was present in normal amounts; there were 9 cells per cubic millimeter and the colloidal gold reaction was negative. This test was repeated with similar results. Six injections of arsphenamin were then given over a period of some months. Five months later another spinal fluid examination was made. This again gave a positive Wassermann reaction with 1 c.c., 0.7 c.c., and 0.5 c.c. of spinal fluid. No cells were found in the specimen examined. Globulin was not obtained, and the albumin was present in normal amounts. The colloidal gold reaction was again negative. Thirteen injections of arsphenamin were given in the next ten months, and a spinal fluid examination at this time showed a positive Wassermann reaction with 1 c.c., 0.7 c.c., and 0.5 c.c. of spinal fluid. Globulin was present; there was an increase of albumin; and a pleocytosis of 25 cells per cubic millimeter was found. The colloidal gold reaction gave a strong paretic curve, reading 5554443211.

Treatment and Course.—In the following eleven months, twenty-four injections of arsphenamin were given. At this time, the spinal fluid gave a doubtful Wassermann reaction, that is, there was a partial inhibition of hemolysis with 1 c.c. of spinal fluid, 0.8 of a c.c. giving a negative reaction. There were 4 cells per cubic millimeter; globulin was present in small amounts, and albumin was slightly increased. The colloidal gold reading was 1143210000, a reaction typical for cerebrospinal syphilis. The patient was given an injection of arsphenamin, and an intraspinal injection of Swift-Ellis serum, fortified by ⅓ mg. of arsphenamin. Two weeks later, another specimen of spinal fluid was examined. The Wassermann test was not made. The cell count was normal. There was a slight amount of globulin, and a small increase in the albumin. The colloidal gold reaction was 1112100000, an almost negative reaction. This examination was followed by two injections of arsphenamin and one intraspinal injection similar to the previous one.

Blood and Spinal Fluid Reactions.—The reactions obtained Aug. 17, 1917, before treatment were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, 5 — — — — — (positive); globulin, 0; albumin, normal; cells, 9 per cubic millimeter; colloidal gold test, negative. After six intra-

1. The Wassermann reaction on the spinal fluid is performed on titrated quantities varying from 1 c.c. to 0.05 c.c. The figure 5 represents strongly positive and a dash (—) a negative reaction. Each figure or dash represents the reaction for a certain dilution, the figure at the left representing the reaction with 1 c.c. of fluid, the second figure in 0.8 c.c., the third in 0.6 c.c. and so on in diminishing amounts. When a zero occurs it means that the test was not made in the dilution represented by its position.

venous injections of arsphenamin the reactions obtained Jan. 18, 1918, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, 5541 —— (positive); globulin, 0; albumin, normal; cells, 0 per cubic millimeter; colloidal gold test, negative. After fourteen intravenous injections of arsphenamin the reactions obtained Nov. 9, 1918, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, 555000 (positive); globulin, +; albumin, ++; cells, 25 per cubic millimeter; colloidal gold test, 5554443211. After twenty-six intravenous injections of arsphenamin the reactions obtained Oct. 21, 1919, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, 3—0000 (doubtful); globulin, +; albumin, ++; cells, 4 per cubic millimeter; colloidal gold test, 1143210000. After two intravenous injections of arsphenamin and one intraspinal injection of arsphenamized serum the reactions obtained Nov. 8, 1919, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, unsatisfactory; globulin, +; albumin, +; cells, 2 per cubic millimeter; colloidal gold test, 1112100000. After three intravenous injections of arsphenamin and one intraspinal injection of arsphenamized serum the reactions obtained Dec. 16, 1919, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, negative; globulin, 1; albumin, 1; cells, 28 per cubic millimeter; colloidal gold test, 5445410000. After six intravenous injections of arsphenamin the reactions obtained April 17, 1920, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, negative; globulin, 1; albumin, 1; cells, 5 per cubic millimeter; colloidal gold test, 3333320000. After two intravenous injections of arsphenamin and one intraspinal injection of arsphenamized serum the reactions obtained May 4, 1920, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, negative; globulin, 2; albumin, 1; cells, 4 per cubic millimeter; colloidal gold test, 5555531000.

Case 3.—*History.*—This patient was seen first in the ataxic state of tabes dorsalis. He gave no history of syphilitic infection, but had been complaining of weakness in the legs and general malaise for about two years. He had been given twelve intravenous injections of arsphenamin at a local dispensary.

Examination.—This showed a classic picture of advanced tabes dorsalis. The pupils were unequal and gave the Argyll Robertson reaction. There was a paresis of the left external rectus muscle. Knee jerks and ankle jerks were absent. The patient was practically bedridden. The Wassermann reaction was negative for the blood and spinal fluid. There were 5 cells per cubic millimeter in the spinal fluid, a slight amount of globulin, and a slight increase of albumin. The colloidal gold reaction was essentially negative, 0000110000.

Treatment and Course.—He was given an intraspinal injection of Swift-Ellis serum, reinforced by 0.0002 gm. of arsphenamin, and one intravenous injection of arsphenamin. The spinal fluid examination two weeks later gave a positive Wassermann reaction down to 0.3 of a c.c. Globulin was absent; albumin was present in normal amounts; there were 3 cells per cubic millimeter, and the colloidal gold reaction was again essentially negative, 0001200000. Another intraspinal injection of the same type as the previous one and four intravenous injections of arsphenamin were given, and in six weeks the spinal fluid was again examined. The Wassermann reaction was doubtful; a slight amount of globulin was present; albumin was increased; there were 3 cells per cubic millimeter, and a fairly strong colloidal gold reaction, 4432210000. Another intraspinal injection of Swift-Ellis serum, reinforced by 0.0001 gm. of arsphenamin and five intravenous injections of arsphenamin

were given, and five weeks later the spinal fluid showed a positive Wassermann reaction with 0.5 of a c.c.; one cell per cubic millimeter; globulin was present; albumin was increased; and a colloidal gold reaction of 4333210000 was obtained. The intraspinal treatment was repeated, reinforcement of arsphenamin being by 0.0003 gm., and another fluid examination was made three weeks later. The Wassermann test was positive with 1 c.c. and moderately positive with 0.7 c.c. and 0.5 c.c. There were 9 cells per cubic millimeter; globulin was present; albumin was increased; the colloidal gold reaction was 4433210000. In the following two months, two further intraspinal treatments were given of the same type as the last, and the spinal fluid again showed a positive Wassermann reaction with 1 c.c. and 0.7 c.c., and doubtful reactions with 0.5 c.c. and 0.3 c.c. There were 6 cells per cubic millimeter; globulin was present; albumin was increased; and the colloidal gold reaction was 1123100000.

Blood and Spinal Fluid Reactions.—The reactions obtained before treatment, June 7, 1919, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, negative; globulin, +; albumin, +; cells, 5 per cubic millimeter; colloidal gold test, 0000111000. After one intraspinal injection of arsphenamized serum and one intravenous injection of arsphenamin the reactions obtained, June 21, 1919, were: Wassermann reaction of the spinal fluid, 55555— (positive); globulin, 0; albumin, normal; cells, 3 per cubic millimeter; colloidal gold test, 0001200000. After one intraspinal injection of arsphenamized serum and four intravenous injections of arsphenamin the reactions obtained, Aug. 2, 1919, were: Wassermann reaction of the spinal fluid, doubtful; globulin, +; albumin, +; cells, 3 per cubic millimeter; colloidal gold test, 4432210000. After one intraspinal injection of arsphenamized serum and five intravenous injections of arsphenamin the reactions obtained, Sept. 9, 1919, were: Wassermann reaction of the spinal fluid, 5551—— (positive); globulin, +; albumin, +; cells, 1 per cubic millimeter; colloidal gold test, 4333210000. After one intraspinal injection of arsphenamized serum the reactions obtained, Sept. 27, 1919, were: Wassermann reaction of the spinal fluid, 543——— (positive); globulin, +; albumin, +; cells, 9 per cubic millimeter; colloidal gold test, 4432210000. After three intraspinal injections of arsphenamized serum the reactions obtained, Nov. 21, 1919, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, 5532—— (positive); globulin, +; albumin, +; cells, 6 per cubic millimeter; colloidal gold test, 1123100000. No treatment was given. The reactions obtained, Dec. 13, 1919, were: Wassermann reaction of the spinal fluid, negative; globulin, +; albumin, +; cells, 2 per cubic millimeter; colloidal gold test, 3432210000. After one intravenous injection of arsphenamin and one intraspinal injection of arsphenamized serum the reactions obtained, Jan. 11, 1920, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, 4——————— (doubtful); globulin, 0; albumin, 0; cells, 4 per cubic millimeter; colloidal gold test, 1111100000. After one intravenous injection of arsphenamin and one intraspinal injection of arsphenamized serum the reactions obtained, Feb. 21, 1920, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, negative; globulin, 0; albumin, 1; cells, 5 per cubic millimeter; colloidal gold test, 1122100000. After one intravenous injection of arsphenamin and one intraspinal injection of arsphenamized serum the reactions, March 20, 1920, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, negative; globulin, 1; albumin, 1; cells, 4 per cubic millimeter; colloidal gold test, 1123210000. After one intra-

spinal injection of arsphenamized serum the reactions obtained, April 17, 1920, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, negative; globulin, 1; albumin, 1; cells, 7 per cubic millimeter; colloidal gold test, 2210000000. After two intravenous injections of arsphenamin and two intraspinal injections of arsphenamized serum the reactions, June 12, 1920, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, negative; globulin, 0; albumin, normal; cells, 2 per cubic millimeter; colloidal gold test, negative.

Case 4.—*History.*—This patient gave a history of a chancre twenty years ago, which was burned with caustic. No secondary symptoms appeared, and he had no further treatment. Nothing of importance occurred until six months ago, when he began to feel dizzy, complained of sharp, shooting pains in the right arm and leg and severe frontal headache, which kept him awake at night. He was also quite dizzy. A short time later he had an attack, which left him weak on the right side, and about a month later his speech became thick. Impotence came on about this time. He went to a local dispensary where he was given fourteen injections of arsphenamin at weekly intervals. When seen by us, he was complaining of about the same symptoms, except that his dizziness was less marked and his headache had disappeared. In addition, he had difficulty in swallowing, "things going down the wrong way," and he was short of breath.

Examination.—The pupils were small, about equal in size and reacted sluggishly to light. There was no nystagmus or strabismus and no diplopia. The right side of the face was drawn up slightly. The tongue protruded in the midline. The right half of the palate was not raised as well as the left. There was a dysarthria; test phrases were pronounced a little heavily and with slurring. The arm reflexes were sluggish, but the right reflex was more pronounced than the left. The knee jerks and ankle jerks were absent. The patient walked with a slight ataxia, and there was marked swaying in the Romberg position. There was subjective numbness of the right hand but no objective sensory disorder. The Wassermann reaction was negative for the blood and spinal fluid. There were no cells in the cubic millimeter of fluid examined; globulin was not present; albumin was present in normal amounts; the colloidal gold reaction was essentially negative, 0000001110.

Course and Treatment.—He was given an intraspinal injection of Swift-Ellis serum, reinforced by 0.0002 gm. of arsphenamin, and five intravenous injections of arsphenamin. The spinal fluid examination, six weeks after the intraspinal injection, showed 13 cells per cubic millimeter. Globulin was present; albumin somewhat increased, and there was a paretic colloidal gold reaction, 5555431000. The Wassermann reaction on the spinal fluid was not done. He was given another intraspinal injection and four intravenous injections. The Wassermann reaction was negative; globulin was present in small amounts; albumin was increased; and the colloidal gold reaction was 5444321000. Another intraspinal injection of Swift-Ellis serum, reinforced by 0.0005 gm. of arsphenamin, was given, and five weeks later the spinal fluid was again examined, showing a negative Wassermann reaction; 1 cell per cubic millimeter; globulin was present; albumin was increased, and the colloidal gold reaction was 5433211000. There had been no subjective improvement in the patient, consequently treatment was discontinued for a time. At the end of two months, the patient had a shock resulting in hemiplegia.

Blood and Spinal Fluid Reactions.—The reactions obtained before intraspinal treatment, June 14, 1919, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, negative; globulin, 0; albumin, normal; cells, 0 per cubic millimeter; colloidal gold test, 0000001110. After one intraspinal injection of arsphenamized serum and four intravenous injections of arsphenamin the reactions obtained, Aug. 2, 1919, were: Wassermann reaction of the spinal fluid, not reported; globulin, +; albumin, +; cells, 13 per cubic millimeter; colloidal gold test, 5555431000. After one intraspinal injection of arsphenamized serum and four intravenous injections of arsphenamin the reactions obtained, Sept. 6, 1919, were: Wassermann reaction of the spinal fluid, negative; globulin, +; albumin, +; cells, 1 per cubic millimeter; colloidal gold test, 5444321000. After one intraspinal injection of arsphenamized serum and one intravenous injection of arsphenamin the reactions obtained, Oct. 11, 1919, were: Wassermann reaction of the spinal fluid, negative; globulin, +; albumin, +; cells, 1 per cubic millimeter; colloidal gold test, 543321000.

CASE 5.—*History.*—The patient was a woman, 37 years of age at the time of the first examination, who had a definite clinical picture of tabes dorsalis. For eight years she had been having sharp pains in the legs which had finally become so severe that she had to give up her work. An ataxic gait had developed, the difficulty in walking being most marked when it was dark.

Examination.—Neurologic examination showed unequal, poorly reacting pupils; absence of knee jerks and ankle jerks; ataxia in walking and a Romberg sign. The serology was interesting; a positive blood Wassermann reaction but a negative Wassermann reaction in the spinal fluid were obtained. There was a suggestion of a globulin ring by the Ross-Jones test but hardly enough to be called a definite reaction. There were 139 cells per cubic millimeter and an almost negative colloidal gold reaction, 0011230000.

Course and Treatment.—Under treatment, consisting of the injection of arsphenamin and mercury, she improved rapidly. The pains practically disappeared, and she found walking less difficult. She was enabled to return to work.

After thirty-two injections of arsphenamin and eight of mercury salicylate a second lumbar puncture was performed. The blood Wassermann reaction was negative, but the spinal fluid gave a strongly positive reaction; globulin was present; the cell count was 30 per cubic millimeter, and the colloidal gold test had become strongly positive, 5444310000.

Blood and Spinal Fluid Reactions.—The reactions obtained before treatment, Jan. 23, 1919, were: Wassermann reaction of the blood, positive; Wassermann reaction of the spinal fluid, negative; globulin, ±; albumin, ±; cells, 139 per cubic millimeter; colloidal gold test, 0011230000. After thirty-two injections of arsphenamin and eight injections of mercury the reactions obtained, Oct. 4, 1919, were: Wassermann reaction of the blood, negative; Wassermann reaction of the spinal fluid, 550000; globulin, +; albumin, +; cells, 30 per cubic millimeter; colloidal gold test, 5444310000.

CASE 6.—*History.*—This case shows the provocative reaction in the ventricular fluid after intraventricular injections. The patient was suffering from taboparesis and was quite demented. He had acquired syphilis about nineteen years before, receiving treatment at that time. He had been deteriorat-

ing mentally for about two years before appearing at the clinic and had received a few injections of arsphenamin but was rapidly becoming worse. He was given intraventricular injections of arsphenamized serum.

Examination. — Examination at the time of the intraventricular injection showed unequal, irregular pupils which did not react to light but did react to accommodation; the knee jerks and ankle jerks were absent; there was a speech defect. He was depressed, memory was poor, calculating ability nil (he was a civil engineer), and he was irritable and emotionally unstable. The spinal fluid was positive in all tests.

On Dec. 15, 1919, a trephine opening was made in the calvarium by Dr. W. J. Mixter at the Massachusetts General Hospital. Fluid was withdrawn from the lateral ventricle and 15 c.c. of Swift-Ellis serum was injected. A lumbar puncture was performed at the same time. The spinal fluid was strongly positive, whereas the ventricular fluid was negative. A second ventricular fluid examination in February, 1920, was again essentially negative. On April 6, 1920, the ventricular fluid showed a relatively strong colloidal gold reaction, 4431000000; all other reactions were negative. However, on May 4, 1920, all tests had become positive, with the exception of the cell count. During this period from December, 1919, to May, 1920, the patient had received fifteen intravenous injections of arsphenamin, one intraspinal injection of arsphenamized serum and four intraventricular injections of serum, three of which were arsphenamized. The patient showed some clinical improvement.

In this case we would appear to have provoked positive reactions in the ventricular fluid.

Ventricular Fluid Reactions.—The reactions obtained, Dec. 17, 1919, before treatment, were: Wassermann reaction of the ventricular fluid, negative; globulin, 0; albumin, normal; cells, 1 per cubic millimeter; colloidal gold test, negative. After two intraventricular injections of arsphenamized serum and eight intravenous injections of arsphenamin the reactions obtained, Feb. 20, 1920, were: Wassermann reaction of the ventricular fluid, negative; globulin, 0; albumin, normal; cells, 0 per cubic millimeter; colloidal gold test, 2100000000. After one intraventricular injection of arsphenamized serum, one intraspinal injection of arsphenamized serum and five intravenous injections of arsphenamin the reactions obtained, April 6, 1920, were: Wassermann reaction of the ventricular fluid, negative; globulin, 0; albumin, normal; cells, 1 per cubic millimeter; colloidal gold test, 4431000000. After one intraventricular injection of arsphenamized serum and two intravenous injections of arsphenamin the reactions obtained, May 4, 1920, were: Wassermann reaction of the ventricular fluid, 522 — — —; globulin, 2; albumin, 2; cells, 1 per cubic millimeter; colloidal gold test, 55553200000.

These cases illustrate the fact that after antisyphilitic treatment a negative spinal fluid may become positive, or one that is slightly positive may give more strongly positive reactions.

In Case 1 the diagnosis was cleared by the effect of a provocative injection of arsphenamin. In this case the spinal fluid, which was negative prior to antisyphilitic treatment, became strongly positive in all tests after one injection of arsphenamin. It is worth while to note that the blood did not become positive. This result is also found in the other cases of this series.

Case 2 of the series shows the intensification of the spinal fluid Wassermann reaction after intravenous injection and also the provocation of a positive colloidal gold reaction, globulin and pleocytosis. It is perhaps of interest to point out in this discussion the curious fact that no provocative change was noted in the serum Wassermann reaction. In the light of present knowledge perhaps one may conclude that the patient is cured so far as visceral involvement is concerned. A latent focus of spirochetes in the nervous system was apparently activated by treatment, as was manifested by the provocative spinal fluid changes. This case is of further interest from the standpoint of conjugal neurosyphilis: paresis in the wife and latent neurosyphilis in the spouse.

The patient in Case 3 presented so definite a picture of tabes that there could be no doubt of the diagnosis, despite a spinal fluid that was negative except for a small amount of globulin and albumin increase. No provocative result occurred either in the blood or spinal fluid as the result of intravenous injection, but intraspinal subdural injections of arsphenamized serum provoked a positive Wassermann and a positive gold reaction. It is worth while to note that under treatment these reactions were reduced to almost normal. From the clinical standpoint, improvement took place even during the period in which the tests became more strongly positive. The patient, confined to bed, in the paralytic state of tabes, became able to walk without a cane, although quite ataxic.

The patient in Case 4 had undoubted tabetic disease, showing negative blood and spinal fluid reactions. Under intraspinal subdural injections the spinal fluid showed positive globulin, albumin, pleocytosis and gold reaction, but the blood and spinal fluid Wassermann tests remained negative. Contrary to the experience in Case 3, no improvement in the patient resulted from this treatment.

Case 5 is that of another patient on whom the clinical evidence made a diagnosis of tabes certain, but whose spinal fluid Wassermann reaction was negative. The blood, however, was positive, and there were 139 cells per cubic millimeter in the fluid. Under intravenous injections of arsphenamin, the Wassermann reaction in the blood serum became negative, while, on the other hand, the spinal fluid Wassermann reaction became positive. The cell count decreased, but the colloidal gold reaction became more strongly positive. From the clinical standpoint, the result of treatment was eminently satisfactory, as all pain disappeared, the ataxia became markedly improved, and the patient was able to return to work, after having been incapacitated for some months prior to treatment.

The patient in Case 6 showed the provocative results in the ventricular fluid after intraventricular injections, similar to those observed in the spinal fluid of the preceding cases.

Altman and Dreyfus [2] have shown that arsphenamin may have a provocative influence on the spinal fluid in cases of primary and secondary syphilis. They examined the spinal fluid in the primary and secondary period of the disease, both before and after the intravenous administration of arsphenamin. One of their cases may be reviewed: A patient who presented no subjective or objective symptoms of nervous involvement and whose spinal fluid was negative, received 0.4 gm. arsphenamin intravenously. He then absented himself from the clinic for a period of seven weeks. When he returned, he presented a facial paralysis and an involvement of the eighth nerve. The spinal fluid at this time showed a high pleocytosis, much globulin and a positive Wassermann reaction in both high and low dilutions of the spinal fluid. The serum Wassermann reaction on both occasions was positive. These writers speak of this phenomenon as a provocative neurorecidive. A criticism of this conclusion might be offered, as it is quite possible that the condition had nothing to do with the introduction of arsphenamin, but might have occurred had it not been injected. As this occurred some time after the injection, and as there was only one injection, this case cannot be considered as strong evidence, but as illustrative of this type of reaction.

A study similar to that of Altman and Dreyfus was made by one of us (J. V. K.).[3] In a series of twenty-five cases of secondary syphilis, the spinal fluid was examined before and after a course of four intravenous injections of arsphenamin, administered at intervals of seven to ten days. Provocative spinal fluid changes were observed in some of the cases on the second examination of the spinal fluid. This observation, and those of Altman and Dreyfus are in accord with the hypothesis of Gennerich,[4] that arsphenamin is capable of provocative spinal fluid changes in the early period of syphilis.

The provoking of a spinal fluid by arsphenamin therapy from negative to positive is, in all probability, the expression of a Herxheimer reaction. A neurorecidive or neurorecurrence following arsphenamin injection is probably a clinical expression of this reaction. The apparent provocative reactions in the spinal fluid of neurosyphilitic patients, as herein reported, would seem to be of a similar nature and in line with the statements made above.

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2. Altman and Dreyfus: München. med. Wchnschr. **60**:464; 531, 1913.

3. Klauder, J. V.: Am. J. Syphilis **3**:559 (Oct.) 1919.

4. Gennerich: Die Liquorveränderungen in den einzelnen Studien der Syphilis, Berlin, 1913.

PROVOCATIVE REACTION NOT FREQUENT

It should be emphasized that this provocative reaction is not a frequent occurrence even in cases in which there is evidence of central nervous system involvement with negative findings in the spinal fluid. This may be illustrated by the following cases:

CASE 7.—The patient, a man aged 36, came to the hospital after an attack of pneumonia, complaining of feeling weak. Examination showed Argyll Robertson pupils and active knee reflexes. The Wassermann reaction was positive in the blood. The spinal fluid reactions were negative. A colloidal gold test was not made at this time. The patient was given antisyphilitic treatment, which was continued for over a year. Four consecutive negative Wassermann reactions of the blood serum were then obtained. A lumbar puncture at this time was again entirely negative, except for the colloidal gold reaction, which gave a paretic type of curve, 5553000000.

CASE 8.—A man, aged 35, who was brought to the hospital because of hallucinations and delusions which were apparently the result of alcoholic indulgence, had acquired syphilis a year before, for which he had been treated, and had been discharged with a negative Wassermann reaction of the blood. On admission to the hospital for his hallucinosis, he gave a negative blood Wassermann reaction and a negative spinal fluid Wassermann reaction but a pleocytosis, excess of globulin and albumin, and a paretic gold reaction. Several intravenous injections of arsphenamin were given for provocative effect, but none was found either in the blood or spinal fluid.

There appears to be some evidence that certain cases of neurosyphilis are made worse by arsphenamin therapy. This matter, which is discussed in numerous places under the heading of neurorecidive or neurorecurrence, has had proponents and opponents in great numbers. It seems to us, however, that there is considerable clinical evidence that occasional cases of neurorecurrence are caused by arsphenamin injection. This is much more frequent, probably, in the secondary period of the disease than later. The reactions to arsphenamin doubtless manifest the powerful spirocheticidal action of the drug. The arsphenamin either activates foci of spirochetes or, as a result of the lysis of great masses of organisms, the toxins are liberated in large amounts, which produces pathologic results. We may then, assume that this result is expressed in a laboratory way by the appearance of provocative reactions in the blood and spinal fluid, and in a clinical way by the appearance of neurorecidives and the accentuation of symptoms.

UNFAVORABLE RESULTS OF THERAPY

The two following cases may be given as illustrations of unfavorable results of therapy:

CASE 9.—The patient was a boy, aged 9 years, with the evidence of congenital syphilis. There were three miscarriages preceding his birth. At an early age he developed snuffles and had a skin rash. The family doctor made

a diagnosis of blood disease, and he was given inunctions of mercury. At the age of 6 he had eye trouble, which was diagnosed as interstitial keratitis. He was given four injections of the diarsenol brand of arsphenamin, 0.15 gm. each, in a period of six weeks. He was then given mercury by mouth. About two weeks after the discontinuance of the arsphenamin, he sustained a left sided paralysis.

CASE 10.—A man, 49 years of age, gave a history of a genital lesion thirty-two years previously. Twenty-five years after the lesion appeared, he began to suffer with acute attacks of indigestion. At that time the onset of his present symptoms began. When seen seven years after the onset of symptoms he was having gastric crises, lancinating pains, sphincter disturbances, girdle sensation, impotence, diplopia and impaired memory. He was given two injections of neo-arsphenamin, 0.9 gm., with a week between the injections. He experienced a severe reaction each time. He was confined to bed for two days after the first injection and for four weeks after the second. He was said to be out of his mind. The pains in his legs became more severe and his speech was affected. A year later he showed some improvement.

While many such cases could be reported, they are not usual, but represent a small minority of all cases. Our purpose in calling attention to them at this time is for comparison with the provocative results shown in the spinal fluid examination of the first five cases of this series.

SPINAL FLUID FINDINGS AS AN INDICATION FOR TREATMENT

Our intention is not to discuss the indications or contraindications for treatment of syphilis or neurosyphilis, but rather to present in concrete form the type of Herxheimer reaction represented by changes in the spinal fluid. Nevertheless, a word may be said concerning the bearing of these findings on the question of treatment. From this standpoint, probably the most important group is that containing cases that may be considered as latent neurosyphilis, that is, cases in which, although there is evidence of syphilitic activity in the nervous system as shown by the spinal fluid findings, the patient is without symptoms. In some instances, as in the second case of our series, the spinal fluid finding may be mild, such as a positive Wassermann reaction only. Was harm done in this case because the reactions became stronger after treatment? It might be stated that a continuation of treatment produced a diminution in these findings; in Cases 3 and 5, good results are to be accredited to treatment, despite the intensification of the spinal fluid findings. In Cases 3 and 5 the treatment was of great value as the patients were in better condition than they were before treatment. Possibly some difference of opinion as to the value of treating patients with latent neurosyphilis will depend on a theoretical difference of opinion. Thus, there is a school of syphilologists who believe that syphilis is an incurable disease and that all that therapy can be expected to accomplish is the production of a latent

condition. Another group, that may be considered as somewhat more optimistic, believes that syphilis is a curable condition, and that a great effort should be made to produce negative serology. It is quite obvious, of course, that both conceptions may be carried to a degree that is not rational. The neurologist will usually hold that the only way to prevent the occurrence of the symptoms of neurosyphilis is to treat the patients intensively before these symptoms have occurred, and it is generally held that the appearance of pathologic findings in the spinal fluid is a certain forerunner of destructive lesions. On the other hand, it would appear advisable to discontinue treatment in cases that are apparently quiescent for years and in which treatment seems to have little effect on the spinal fluid findings and which do not show any clinical improvement.

We should like to make clear, in conclusion, that these provocative changes and the cases in which, from the clinical standpoint, the condition becomes worse after treatment, are, in reality, few in number and not of sufficient frequency to cause concern.

SUMMARY

Case histories are given to show that after treatment the cerebrospinal fluid, which was negative before treatment, may become positive in all routine tests, or a weakly reacting fluid may become much stronger. This is called a provocative reaction. It may be accomplished by the intravenous or intraspinal injection of arsphenamin. This is compared to the Herxheimer reaction or the production of neurorecurrences and is considered as the laboratory analogue. The provocative reactions are shown to occur in both the ventricular and spinal fluids. This is not a frequent phenomenon, and patients with vascular neurosyphilis with negative cerebrospinal fluids may not react in this manner. However, diagnosis may occasionally be made clear in obscure cases. In none of the cases in this series was the provocative reaction obtained with the blood serum. Despite the increase in the strength of the spinal fluid reactions, clinical improvement may result, and continued treatment may again produce a negative fluid.

A CLINICAL STUDY OF THE REACTIONS FOLLOWING THE INTRAVENOUS ADMINISTRATION OF ARSPHENAMIN IN NONSYPHILITIC PERSONS*

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Ten years have now elapsed since arsphenamin (salvarsan) was first introduced by Paul Erlich and his associates, and during that space of time many thousands of doses of this remedy have been administered. Almost from the beginning and extending to the present, untoward symptoms have been noted following the intravenous administration of arsphenamin. Many hypotheses have been advanced to explain these reactions, but as yet no method has been suggested which would eliminate these untoward reactions.

In this study, arsphenamin (Dermatological Research Laboratory) of the same serial number was administered to both syphilitic and nonsyphilitic patients, and the reactions following their intravenous administration were noted. It was believed that a study of this nature might throw some light on the possible cause or causes of these untoward symptoms.

SYMPTOMS IN SYPHILITIC AND NONSYPHILITIC PATIENTS

The reactions following the intravenous administration of arsphenamin are classified into: (1) immediate, (2) early, and (3) late symptoms. We shall concern ourselves in this discussion with a study of the early symptoms which were noted following the intravenous administration of arsphenamin to the nonsyphilitics and compare them with the symptoms observed when the identical product was administered to syphilitic patients.

The symptoms observed in the nonsyphilitic series were headache, chills, fever, nausea, vomiting, diarrhea, and backache. Two patients

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of this series developed cutaneous manifestations; one of the eruptions was scarlatinoid in character, and the other presented the characteristics of a vesicular eczema. Both patients made uneventful recoveries.

In all, 114 injections were administered to nonsyphilitic patients. Table 1 details the results obtained in our syphilitic series.

TABLE 1.—Reactions to Arsphenamin in Normal Persons

Case	Lot	Dose	Reaction
1	3586	0.5	No reaction
2	2586	0.5	Fever, chills, headache, nausea, vomiting, pains in stomach
3	3586	0.5	No reaction
4	3586	0.5	Chills, nausea, loose bowels, no appetite
5	3586	0.5	Chills, fever
6	3586	0.5	Slight fever and loose bowels
7	3586	0.5	Slight nausea
8	3586	0.5	Chills and headache
9	3586	0.5	Headache, nausea, loose bowels, backache
10	3586	0.5	Slight chills and headache, nausea, loose bowels
11	3586	0.5	No reaction
12	3586	0.5	Chills, headache, nausea, loose bowels, no appetite
13	3586	0.5	Headache
14	3586	0.5	Fever, chills, headache, nausea, loose bowels
15	3586	0.5	Fever, chills, headache, nausea
16	3586	0.5	No reaction
17	3540	0.45	Fever, chills, headache
18	3540	0.45	Fever, chills, headache, nausea, loose bowels
19	3546	0.5	Chills, headache, nausea, vomiting, loose bowels, no appetite
20	3546	0.5	No reaction
21	3546	0.5	Headache, nausea, loose bowels
22	3546	0.5	Chills, headache, nausea, loose bowels
23	3546	0.5	Fever, chills, headache, nausea, vomiting, loose bowels
24	3546	0.5	Nausea, loose bowels
25	3546	0.5	Nausea
26	3855	0.5	Fever, chills, headache, nausea, loose bowels, aching of kidneys
27	3855	0.5	Fever, headache, nausea, vomiting at hospital, loose bowels
28	3855	0.5	No reaction
29	3855	0.5	No reaction
30	3843	0.5	Chills, headache, nausea, loose bowels, dizzy
31	3843	0.5	Fever, headache, loose bowels
32	3843	0.5	Nausea, vomiting, sleepy
33	3829	0.5	No reaction
34	3829	0.5	No reaction
35	3829	0.5	No reaction
36	3829	0.5	No reaction
37	3829	0.5	Nausea
38	3829	0.5	Fever, headache
39	3829	0.5	Headache, nausea
40	3829	0.5	Fever, nausea
41	3829	0.5	Chills (little)
42	3829	0.5	Headache (slight)
43	3829	0.5	Slight fever and headache
44	3829	0.5	Nausea
45	3829	0.5	Chills, nausea, vomiting
46	3829	0.5	No reaction
47	3829	0.5	Fever, chills, nausea, loose bowels
48	3829	0.5	Headache, vomiting, loose bowels, backache
49	3829	0.5	Nausea
50	3829	0.5	Fever, chills, headache, nausea, vomiting, loose bowels
51	3829	0.5	No reaction
52	3829	0.5	No reaction
53	3829	0.5	No reaction
54	3829	0.5	Slight nausea, backache
55	3829	0.5	No reaction
56	3829	0.5	Fever, headache, vomiting, loose bowels
57	3829	0.5	No reaction
58	3829	0.5	Chills, headache
59	3829	0.5	No reaction
60	3829	0.5	No reaction
61	3829	0.5	Headache, nausea, loose bowels
62	3884	0.5	Fever, chills, nausea, loose bowels
63	3884	0.5	Chills, nausea and loose bowels
64	3884	0.5	No reaction
65	3805	0.6	Loose bowels
66	3805	0.6	No reaction

TABLE 1.—Reactions to Arsphenamin in Normal Persons—(*Continued*)

Case	Lot	Dose	Reaction
67	3900	0.5	Headache
68	3900	0.5	Headache, nausea, vomiting, loose bowels
69	3878	0.6	Fever, chills, headache, nausea, vomiting, loose bowels
70	3903	0.6	Chills, loose bowels
71	3903	0.6	Nausea, loose bowels
72	3895	0.5	Chills, headache, nausea, loose bowels
73	3895	0.5	Headache
74	3895	0.5	Headache, nausea, vomiting, loose bowels, backache
75	3895	0.6	Fever, chills, headache, nausea, vomiting
76	3895	0.5	No reaction
77	3895	0.6	Fever, chills, headache, nausea, loose bowels, weak and nervous
78	3895	0.5	Fever, chills, headache, nausea, vomiting, loose bowels
79	3900	0.5	Headache, nausea, loose bowels, pain in shoulder blade
80	3900	0.5	Chills
81	3900	0.5	Headache
82	3900	0.5	Headache, nausea, vomiting, loose bowels
83	3900	0.5	Chills, nausea
84	3900	0.5	No reaction
85	3900	0.5	Vomiting, constipation
86	3900	0.5	No reaction (drowsy)
87	3900	0.5	Headache, nausea
88	3900	0.5	Fever, chills, headache, nausea, vomiting, loose bowels
89	3900	0.5	Headache
90	3900	0.5	Loose bowels
91	3928	0.45	No reaction
92	3928	0.45	No reaction
93	3937	0.6	No reaction
94	3928	0.6	Headache, loose bowels
95	3903	0.5	Headache, nausea, loose bowels
96	3903	0.5	No reaction
97	3903	0.5	Loose bowels
98	3903	0.5	No reaction
99	3903	0.5	No reaction
100	3903	0.5	Nausea, vomiting, loose bowels
101	3903	0.5	No reaction
102	3903	0.5	Fever, headache and loose bowels
103	3903	0.5	No reaction
104	3937	0.5	Nausea, loose bowels
105	3937	0.5	Loose bowels
106	3937	0.5	No reaction
107	3937	0.5	Fever
108	3937	0.5	No reaction
109	3937	0.5	Headache
110	3937	0.5	Loose bowels
111	3937	0.5	Loose bowels
112	3937	0.4	Loose bowels (slightly)
113	3937	0.5	No reaction
114	3855	0.5	Loose bowels

Of this number seventy-seven, or 67 per cent., gave evidence of some reactive symptoms. Twenty-five, or 32 per cent., complained of fever; thirty-one, or 40 per cent., of chills or chilliness; forty-six, or 60 per cent., of headache; forty-seven, or 60 per cent., of nausea; eighteen, or 23 per cent., of vomiting; forty-six, or 60 per cent., of diarrhea, and five, or 6 per cent., of backache.

Table 2 gives in detail the reactions reported by the syphilitic patients, receiving the arsphenamin of the same serial numbers as the nonsyphilitic patients. The symptoms complained of were identical in both classes of subjects.

In all, the records of the reactions of ninety-three syphilitics were tabulated. Of this number, sixty-two, or 66⅔ per cent., reported some evidence of reaction. Twenty-five, or 40 per cent., complained of

fever; twenty-six, or 42 per cent., of chills and chilliness; thirty-seven, or 60 per cent., of headache; thirty-seven, or 60 per cent., of nausea; twenty-six, or 40 per cent., of diarrhea; eleven, or 18 per cent., of vomiting and four of backache.

TABLE 2.—Reactions to Arsphenamin in Syphilitic Persons

Case	Lot	Dose	Reaction
1	3586	0.5	No reaction
2	3586	0.5	Fever, chills, headache, nausea, loose bowels, pains in body
3	3586	0.5	No reaction
4	3540	0.5	No reaction
5	3540	0.5	No appetite
6	3540	0.5	No reaction
7	3540	0.5	Slight chills, nausea and loose bowels
8	3546	0.5	Headache, heart and body hurts her
9	3546	0.5	Headache
10	3547	0.5	No reaction
11	3546	0.5	Chills, nausea, loose bowels, heart-burn
12	3855	0.5	No reaction
13	3855	0.5	No reaction
14	3855	0.5	Chills, headache, body hurts and face is swollen
15	3855	0.5	Fever, chills, headache, nausea, loose bowels, pains through body
16	3855	0.5	Fever, headache, stiff joints
17	3855	0.5	Vomiting, tired feeling in back, also slight pains
18	3855	0.5	Fever, chills, nausea, loose bowels, nervous
19	3855	0.5	Chills, headache, nausea, pains in legs
20	3843	0.5	Fever, chills, headache
21	3843	0.5	Headache, loose bowels, feet hurt
22	3843	0.5	Fever, headache, stiff joints
23	3843	0.5	No reaction
24	3843	0.5	Nausea, nervousness
25	3829	0.45	No reaction
26	3829	0.45	Fever, headache, constipated, stiff joints
27	3829	0.5	Headache
28	3829	0.45	No reaction
29	3829	0.45	Chills, headache, nausea, vomiting
30	3829	0.45	Nausea, itching on calf and shins
31	3829	0.45	No reaction
32	3829	0.5	Headache, nausea, vomiting
33	3829	0.45	Fever, chills, headache, loose bowels
34	3829	0.5	Chills, nausea, vomiting, loose bowels
35	3829	0.45	Fever, chills, headache, nausea, loose bowels, pains in body
36	3829	0.5	No reaction
37	3829	0.45	No reaction
38	3829	0.5	No reaction
39	3829	0.5	Chills, headache, nausea, pains in legs
40	3829	0.5	Fever
41	3829	0.5	Fever, chills, nausea and loose bowels
42	3829	0.5	Headache, nausea, loose bowels
43	3829	0.5	Loose bowels
44	3829	0.5	Vomiting, dull feeling in head, tired limbs
45	3884	0.5	Headache, nausea, vomiting
46	3884	0.5	Headache, nausea, loose bowels
47	3884	0.5	Fever, chills, headache, loose bowels
48	3884	0.5	Chills, headache, nausea, loose bowels
49	3884	0.5	Nostril trouble
50	3895	0.45	Fever, headache, nausea
51	3895	0.45	Nausea, loose bowels
52	2895	0.45	Nausea, vomiting, loose bowels, tired in limbs
53	3900	0.45	Headache
54	3900	0.45	No reaction
55	3900	0.45	No reaction
56	3878	0.3	No reaction
57	3878	0.3	Chills, headache
58	3903	0.4	No reaction
59	3903	0.4	Fever, headache, nausea, weakness, pains in knees
60	3895	0.5	Fever, chills, headache, nausea
61	3895	0.5	(Spitting)
62	3895	0.5	Fever, headache, joints ache
63	3895	0.4	Fever, headache, nausea, loose bowels
64	3895	0.5	No reaction
65	3895	0.45	No reaction
66	3895	0.4	Vomiting, loose bowels, tired feeling in limbs
67	3895	0.5	No reaction
68	3895	0.5	No reaction

TABLE 2.—Reactions to Arsphenamin in Syphilitic Persons—(*Continued*)

Case	Lot	Dose	Reaction
69	3895	0.5	Fever, chills, headache, nausea, loose bowels (arm swollen and sore)
70	3895	0.4	Headache, nausea, loose bowels
71	3895	0.5	Chills, nausea, pains in back
72	3895	0.4	Fever, chills, headache, nausea, vomiting
73	3895	0.5	Pains over eyes
74	3900	0.5	Fever, chills, headache, nausea, loose bowels
75	3900	0.5	Nausea, pains in chest and shoulders
76	3900	0.5	Fever, headache, nausea, loose bowels
77	3900	0.5	Fever, chills, nausea
78	3900	0.5	No reaction
79	3928	...	Chills, headache
80	3928	0.4	No reaction
81	3928	...	No reaction
82	3937	0.4	Nausea, vomiting
83	3937	0.4	Loose bowels
84	3937	0.4	No reaction
85	3928	0.4	Fever, chills, headache, nausea, vomiting, pains in the legs
86	3928	0.4	Nausea
87	3928	0.4	Weak
88	3903	0.45	Nausea
89	3903	0.45	Fever, chills, headache, loose bowels
90	3903	0.45	Feels tired
91	3903	0.45	Headache, nausea, loose bowels
92	3937	0.45	No reaction
93	3937	0.45	No reaction

It is to be noted from the study of these tables that the percentage of reactions was equal in both the syphilitic and nonsyphilitic series. The statistical analysis of the tables recorded shows these results:

Fever as a symptom was recorded in 40 per cent. of the syphilitic patients and in 32 per cent. of the nonsyphilitics; diarrhea in 60 per cent. of the nonsyphilitics and in 40 per cent. of the syphilitics; chills in 40 per cent. of the nonsyphilitics and in 42 per cent. of the syphilitics; vomiting in 23 per cent. of the nonsyphilitics and in 18 per cent. of the syphilitics, and headache and nausea occurred in 60 per cent. of both the syphilitic and nonsyphilitic patients.

It will be noted that the percentages of the reactive symptoms registered approach one another so closely in the syphilitic and nonsyphilitic series that no definite conclusions can be drawn from the figures per se.

CAUSES OF REACTIONS

The causes of the reactions following the intravenous administration of arsphenamin can be classified into: (1) factors relative to the patient; (2) factors relative to the technic, and (3) factors relative to the chemical compound employed.

1. *Factors Relative to the Patient.*—There can be but little doubt that the mental state of a patient at the time of treatment influences the occurrences of reactive symptoms. Not only is this true of the intravenous injections of arsphenamin but also of mercurial preparations and other medicinal substances which at times are administered intravenously.

One of us (A. Strickler) gave a series of intravenous mercurial injections to a group of syphilitic patients that had received a large number of arsphenamin treatments. A percentage of these patients that had received these mercurial injections reported some of the reactive symptoms, such as headache, nausea, and chilliness which occur after injections of arsphenamin. Similar reactive symptoms were also reported by patients suffering from nonsyphilitic dermatologic affections who had received intravenous injections of mercurial preparations.

2. *Factors Relative to the Technic.*—Under this caption belongs the discussion of the water error of Wechselmann. Wechselmann believed that water impurities, chiefly bacterial proteins, were largely responsible for febrile and gastro-intestinal reactions. Gennerich believed that organic contamination of water by saprophytes was the cause of a certain number of unfortunate consequences.

In 1910, Neisser advanced the view that the febrile symptoms were due to the rapid destruction of innumerable spirochetes and the setting free of endotoxins which reached the blood stream and induced the symptoms. E. H. Martin, in a discussion of the treatment of syphilis, believed that the temperature and bowel symptoms were due to the endotoxins liberated from killed spirochetes, and nausea and vomiting caused by idiosyncrasy.

Our clinical investigation seems to disprove the views of Neisser. Our records show definitely that the reactive symptoms were just as numerous among the nonsyphilitics that had received intravenous injections of arsphenamin, as among the syphilitic patients that received the same medicament of the same serial number. Our evidence seems to point to the fact that the so-called "syphilitic state" of the patient plays either no rôle or a very minor rôle in the causation of reactive phenomena. There are other faults in technic which at times may be responsible for some reactive symptoms, such as the temperature of the water employed, acidity or excessive alkalinity of the solution, too rapid infusion of the solution and the preliminary preparation of the patient.

3. *Factors Relative to the Medicament.*—We are of the impression that the most important factors in the causation of the reactions following the intravenous injections of arsphenamin are to be found: (*a*) in impurities in the drug, and (*b*) in the chemical reactions which probably take place between the arsphenamin and the chemical constituents of the blood.

Arsphenamin is an extremely complex substance, and before its final elaboration numerous intermediate products must be prepared. Arsphenamin cannot be regarded as an absolutely pure compound

because it cannot be purified by repeated crystallization. Arsphenamin does not give arsenic values quite up to the theoretical amount, and furthermore, there are elements present which have no place in the chemical formula. Analyses have shown that arsphenamin contains on the average from 1 to 2 per cent. of sulphur. In view of these statements, it is entirely possible that a medicinal substance, which requires numerous steps for its preparation before its final elaboration, and which is of such complexity, should be capable of producing untoward symptoms when introduced into the blood stream.

SUMMARY

1. Both syphilitic and nonsyphilitic patients may experience similar reactions following the intravenous injections of arsphenamin.

2. The endotoxins, produced presumably by the rapid killing of spirochetes in the blood stream of syphilitic patients, play either no rôle or a very unimportant one in the causation of reactive symptoms.

3. The percentage of reactive symptoms following intravenous injections of arsphenamin is equal in both syphilitic and nonsyphilitic patients.

4. It is our impression that the two most important factors in the production of arsphenamin reactions are (1) the patient and (2) the medicament.

5. Of these two factors, the medicament is far more potent in causing reactive symptoms; the untoward phenomena may be produced either by some impurity in the arsphenamin or by some chemical reaction between the arsphenamin and the chemical constituents of the blood, or both factors may be operative at the same time.

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EFFECTS OF ARSPHENAMIN ON RENAL FUNCTION IN SYPHILITIC PATIENTS *

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CHARLOTTE, N. C.

A short time after arsphenamin came into prominence, renal impairment following its administration was noted in a small percentage of cases. During the first year of its use, Ehrlich [1] called attention to the fact that it should be given judiciously to patients suffering from nephropathies other than syphilitic nephritis. In 1911,[2] Mohr reported three cases of serious renal complications following its use. Two years later, Schlasberg [3] reported twenty-seven cases in all of which albumin and casts developed in the urine. This he attributed to the drug. In order to prove his contention, he injected a number of rabbits and produced in them an experimental nephritis. Other cases have been reported by Geronne, Jadassohn, Scholtz,[4] Wechselmann [5] and others. Wechselmann called particular attention to the deleterious effects on pregnant women and advised Schlayer's lactose test as a precautionary measure in all such cases before administering treatments.

No doubt the drug is more perfect today than it was at that time, and therefore it is less toxic. Perhaps the technic employed then may have been a contributing factor. With our present-day technic and with the perfection of the drug, there are still some patients who develop nephritis after the administration of arsphenamin. The number of such cases cannot be ascertained from the meager literature on the subject. Their occurrence, however, is frequent enough to warrant periodic urine examinations in every patient receiving arsphenamin. As stated by Schlasberg, the microscopic examination should not be omitted since albumin may or may not be present, whereas any marked damage will be detected by the appearance of casts in the sediment. Guy [6] has recently reported observations on 3,000 soldiers who received

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* From the Crowell Urological Clinic.

1. Ehrlich, quoted by Mohr, R.: Med. Klin. **7**:596, 1911.

2. Mohr, R.: Med. Klin. **7**:613, 1911; abstr. J. A. M. A. **56**:1517 (May 20) 1911.

3 Schlasberg: Nord. med. Ark. **45**:1844, 1913; abstr. J. A. M. A. **61**:910 (Sept. 13) 1913.

4. Quoted by Mohr (Footnote 2).

5. Wechselmann, W.: München. med. Wchnschr. **51**: 1845 (Aug. 25) 1914; abstr. J. A. M. A. **63**:1431 (Oct. 17) 1914.

6. Guy, W. H.: Reactions Following the Administration of Arsphenamin: Report of Reaction in a Series of Twenty-Five Thousand Injections, J. A. M. A. **73**:901 (Sept. 20) 1919.

25,000 arsphenamin injections. He saw one death from nephritis, and thirty patients developed transient albuminuria, three of whom had numerous red blood cells and large granular casts in the urine. All of these cases developed after treatments had been administered on a day when all patients reacted. He does not attribute this to the drug but to impurities contained in the water. He draws his conclusions from the fact that he was able to use a drug of the same serial number on other occasions without reactions. Stokes and Busman [7] offer the explanation that the group of reactions reported by Guy might have been due to the rubber tubing. Their cases simulated those described by Guy with the exception that they did not observe any signs of renal complications.

It cannot be denied that in a certain percentage of cases there is some renal damage produced by arsphenamin as shown by Pearce and Brown.[8] Whether these cases of nephritis are caused by arsphenamin or whether they are latent and are only lighted up by the drug, are questions of mere speculation. In order to determine whether all patients might not show some renal functional disturbances following arsphenamin treatments, we picked a number of young men whose average age was 25 years and who so far as we were able to determine had no renal disturbance whatever before treatments were instituted.

TESTS AND RESULTS

As indicators of the influence that arsphenamin might have on renal function, determinations were made of the urea content of the blood by the Van Slyke and Cullen [9] modification of Marshall's urease method and of phenolsulphonephthalein excretion by way of the kidneys by means of the method of Rountree and Geraghty.[10] It was believed that these two tests performed both before and after treatment, together with a careful urinalysis made at the same time, would point out any definite alteration in renal function if such were produced. All tests in order to be comparable were performed by the same method in detail, under the same circumstances as far as possible, and read by the same observer. The phenolsulphonephthalein was administered by the intramuscular route. The initial function test was made the day before or on the day of the first treatment; the final test was made the day following the last injection of the course.

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7. Stokes, J. H., and Busman, G. J.: Tubing as a Cause of Reaction to Intravenous Injection, Especially of Arsphenamin: Preliminary Report, J. A. M. A. **74**:1013 (April 10) 1920.

8. Pearce, Louise, and Brown, W. H.: J. Exper. M. **22**:517, 1915.

9. Van Slyke and Cullen: J. Biol. Chem. **19**:211, 1914.

10. Rountree, L. G., and Geraghty, T. J.: J. Pharmacol. and Exper. Therap. **2**:579, 1910.

For obvious reasons four nephritics with syphilis coming under observation at this time were not included in the group. The case of one of these patients will be reported separately as a case of acute syphilitic nephritis; another was a case of chronic nephritis in a man past middle age; and the other two were in young men who were discovered to have a definite nephritis after having had some treatment and who may have had a pre-existing nephropathy. Owing to the fact that our patients were not hospitalized it was difficult to obtain complete data on all cases and therefore a portion of our work had to be discarded.

In twenty patients on whom phenolsulphonephthalein determinations were made both before and after a course of six arsphenamin injections with a total dosage of 2.7 gm., the average phenolsulphonephthalein excretion before treatment was 51.9 per cent. for two hours as compared with 47.7 per cent. excretion after completing treatment. Five, or 25 per cent., showed a reduction of from 10 to 17 per cent. each, while the other fifteen, or 75 per cent., remained the same at both determinations or showed only a slight reduction after treatment. Only one patient showed a higher phenolsulphonephthalein excretion. The urea content of the blood in twenty cases showed an average of 30.7 mg. per 100 c.c. before treatment, and 34.4 mg. after treatment, while one showed an increase of 19 mg. Four cases, or 20 per cent., remained the same, while three, or 15 per cent., showed a decrease of 1 to 3 mg. each. On the whole the changes in 75 per cent. were not significant.

In forty-four cases in which only the first phenolsulphonephthalein was secured the average excretion for two hours was 53.1 per cent.—closely comparable to the 51.9 per cent. in the twenty cases mentioned. In twenty-eight cases in which the phenolsulphonephthalein test was not performed until the treatment was completed, the average excretion was 49 per cent., closely resembling the final phenolsulphonephthalein excretion of 47.7 per cent. in the group previously mentioned.

The question as to whether those patients receiving two arsphenamin injections a week would show a definite variation from the results obtained with the patient receiving injections at weekly intervals, led us to separate a group of patients treated twice a week with the same total dosage. The results in this group were outlined in the accompanying table.

It is noteworthy that the resulting figures in this table do not vary greatly from those obtained in the cases less intensively treated. These nine patients showed an average phenolsulphonephthalein excretion treatment of 50.4 per cent. and an excretion of 44 per cent. after treatment. The blood urea figures are 33.7 mg. and 35.3 mg., respectively. Three, or 33⅓ per cent. of the cases showed a phenolsulphone-

phthalein reduction of from 10 to 17 per cent. each, although there was no other clinical or laboratory evidence of impaired renal function. The blood ureas showed very little change, but there was a tendency to be higher after treatment.

RESULTS IN A GROUP OF PATIENTS TREATED TWICE A WEEK

Patient	Age	Diagnosis Syphilis	Wassermann Reaction	Phenolsulphonephthalein Excretion		Blood Urea	
				Before	After	Before	After
1. P. B. S.	27	Primary	++++	42 - 10 / 52	29 - 12 / 41	32	36
2. Sch.	31	Primary	++++	33 - 18 / 51	38 - 12 / 50	36	40
3. E. L. C.	50	Primary	Negative	27 - 20 / 47	25 - 17 / 42	36	34
4. W. W. B.	25	Secondary	++++	25 - 16 / 41	15 - 25 / 40	32	37
5. H. H.	20	Primary	Negative; dark-field, positive	31 - 16 / 47	22 - 10 / 32	27	31
6. J. Q. H.	16	Primary	Negative; dark-field, positive	38 - 20 / 58	29 - 12 / 41	32	31.2
7. B. F. R.	30	Tertiary	++++	34 - 17 / 51	37 - 14 / 51	34	37.2
8. P. T.	24	Primary	++++	34 - 19 / 53	23 - 25 / 48	43	43
9. W. S.	40	Primary	++++	39 - 15 / 54	34 - 16 / 50	31.2	28.2
Average 9 cases				50.4	44	33.7	35.3

The patient with acute syphilitic nephritis, previously mentioned, who was under observation at this time, showed an initial high blood urea reading which rapidly declined under arsphenamin treatment, illustrating presumably the beneficial effect of arsphenamin on this type of nephritis. On the other hand, the phenolsulphonephthalein excretion, which was rather high to begin with, declined somewhat during the treatment in spite of the obvious renal improvement as evidenced by the decline in the blood urea content and the disappearance of the albumin. These findings suggest that the admitted inadequacy of the phenolsulphonephthalein test to detect acute nephritides applies also to syphilitic nephritis.

Recently, we have supplemented the other test with blood creatinin determinations. Since we do not have parallel determinations with this test, our results so far do not permit of comparisons and the report of our findings must be withheld until a later date.

PENICILLIUM BREVICAULE VAR. HOMINIS SACCARDO, 1877, BRUMPT AND LANGERON, 1910, IN AN AMERICAN CASE OF RINGWORM OF THE TOES *

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In 1910 Brumpt and Langeron [1] recorded two cases of ringworm of the toe-nails from which they obtained the species of coco-brown fungus above indicated. Last year (1919) Wile and Gaudin [2] made a very brief report of thirteen cases of onychomycosis, seven of which furnished *P. brevicaule*. These are the only cases I have been able to locate in the literature in which this organism is concerned, and I believe therefore that it is the first time it has been reported in an American.

BRUMPT AND LANGERON'S CASES

The disease had been present for ten years on the right great toe of a man, aged 32 years. It had also existed on the right second toe of his mother, aged 68, for fifteen or twenty years. In extemporaneous potash preparations Brumpt and Langeron found mycelia, chlamydospores and conidia; they stated that the filaments recalled those of Madurella and Indiella.

They cultivated the organism pure (except for staphylococci) on each of five trials. It grew easily on usual mold medium at room temperature, became coco-brown, and under the microscope showed the penicillium type of sporangia, brown lemon-shaped or spherical conidia (spores) and vesicles on the mycelia. Brumpt and Langeron's text-book description is naturally short, but it implies that they made a deeper study which appears to deserve a more detailed report, but if this was ever made, I have been unable to locate it. I can confirm all their observations; which are easily sufficient, taken with their illustrations of the fungus, to satisfy any one that the organism I have cultivated is the same as theirs. They conclude by saying that this is the first penicillium to be observed in a lesion and subsequently

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* From the Laboratory of Dermatological Research, Department of Cutaneous Medicine, University of Pennsylvania.

1. Brumpt and Langeron: Precis de Parasitologie, Paris, Masson et Cie, 1910, p. 838.

2. Weil, P. E., and Gaudin, C.: Compt. rend. Soc. de biol. **82**: 121, 1919.

cultivated in the hanging drop. This indicates how unusual it is to cultivate this ubiquitous genus (penicillium) of fungi when pathogenic, even though it has been observed in several (for the most part tropical) diseases (Figs. 1 and 2).

WEIL AND GAUDIN'S CASES

These authors reported thirteen cases out of some hundreds of patients examined. They stated that the species of fungus at fault could not be predicated from clinical appearances, and that the

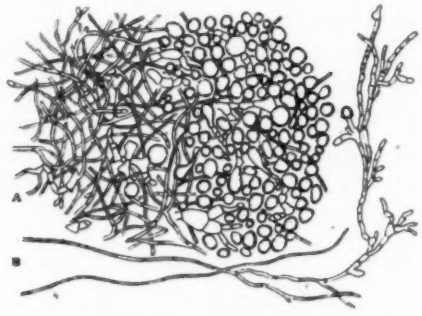

Fig. 1.—Reproduction from Brumpt. Appearance of the fungus in scrapings. A, from first case; B, from second.

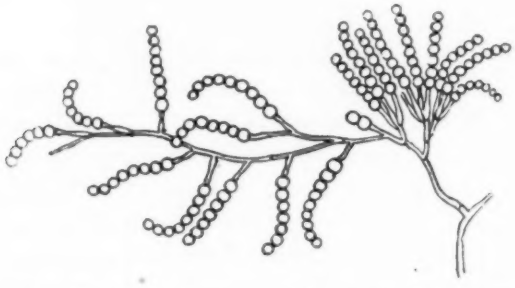

Fig. 2.—Reproduction from Brumpt. Schema of the fungus in culture.

hypertrophic form of onychomycosis could proceed to the grade of onychogryphosis. From the laboratory side they stated that (unlike Brumpt and Langeron) they obtained many kinds of molds in cultures. They gave no details of methods, only the cultural results. These were: *P. brevicaule*, six cases; *Scopulariopsis* (sp.?), one case; *Spicaria* (sp.?), four cases (associated in one with *P. brevicaule*); *Sterigmatocystis*, five cases.

AUTHOR'S CASE

History.—W. H. K., a white man, aged 64, a shoemaker, invalided by chronic valvular cardiac disease, in addition to cardiac symptoms had developed in the past two months a persistent, furiously itching, dry scaly eczema around the waist, which I ascribed to digitalis medication. Scrapings from these positions showed no fungi.

The condition on his toes had endured over thirty years and had never given him any trouble. He stated that from time to time the great toe nails had dropped off and slowly regrown. He recalled no injuries to these parts.

Examination.—On examination it was found that all of his nails lacked the normal luster, but that only three of them were diseased. Both great nails were thickened and lusterless. Their free edges were underlaid by crumbly keratin, and the upper surface was uneven as though from erosion. Flakes and lamellae of keratin on the surface had a pale, coco-brown color. The second toe of the left foot was also opaque and thickened, but in other respects differed materially from the others. It was black, the surface was smooth and the whole nail so loose that only a little force was necessary to remove it bodily from its matrix (Fig. 3).

Fig. 3.—The toes before avulsion of the second left toe-nail (author's case).

Microscopic Examination of Scrapings.—On the first occasion the material was selected from the crumbly matter beneath the free margin of the right great toe. To my suprise no mycelia, but double-contoured bodies were discovered which suggested the possibility of blastomyces (Fig. 4). In a second preparation very fine mycelia were found (Fig. 5). On a second occasion I examined material from all three of the diseased toes. This time mycelia were found in all, and some of the double contoured spores in addition in the material from the right great toe, i. e., in the same location they were found in before. There was, as usual in toe-nail scrapings, nothing characteristic about the mycelium which could not be explained on the basis of variations in involution. In some preparations it was broad and in others narrow, according to the differences in age, sufficiency of nutrition and vigor of growth of different specimens. On a third occasion all ten nails were examined. This time the double contoured conidia were found in the two largest toes of the right foot, and nowhere else. Mycelia and small spores were found here and also in the other great toe.

Fig. 4.—Scrapings treated with 10 per cent. sodium hydroxid solution and examined fresh. Note double contour of the spores.

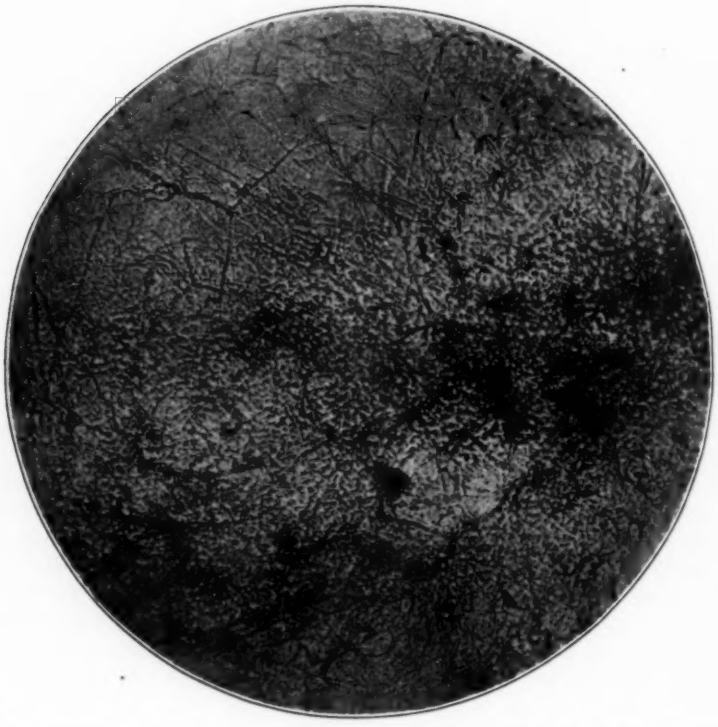

Fig. 5.—Scrapings in 10 per cent. sodium hydroxid solution. Very low power, showing delicate character of mycelium.

The double contoured conidia, as found in extemporaneous potash preparations, were for the most part scattered in small groups through the preparation, but occasionally in denser masses. I have never observed them in penicillium branchings here in scrapings, however, as did Brumpt. They measured from 6 to 8 mm. in diameter, were faintly yellow, spherical and had a thick double membrane. The interior was hyaline and structureless, in others finely granular.

On careful examination, some of the spores (those lying in the appropriate plane) exhibited a slight flattening or pouting at one point which corresponds to its point of attachment to the original mycelium from which it sprang. It thus came to take on something of the appearance of a huckleberry, and reminded one of the operculation seen in ova of some of the parasitic worms (Fig. 11).

CULTURAL STUDY

Three series of cultures were made directly from the case at about monthly intervals. The first was from scrapings under the right great toe nail, the second from the three diseased nails, and the third from all ten nails—the scrapings from each nail being cultivated separately. From the first series a number of obvious contaminants (*Pencillium glaucum*, etc.) was obtained, and *P. brevicaule*. From the second and third series no less than nine different species of mold were obtained—consistently the same in each toe in each of the two examinations; but *P. brevicaule* was not obtained in the two latter series. Of the nine species, several were common saprophytes, but others appeared strange and have not been sufficiently worked up to report on. The details of *P. brevicaule* have been worked out, however, and the chief purpose of this paper is to record them.

Method and Materials.—This description is based on cultures made on plain, glucose, Sabouraud's proof, and Sabouraud's peptone (conservation) agars and on Petroff medium. The organism was grown in various sized test tubes, Petri dishes and hanging agar block (microscopic) preparations. I have insured purity of culture by using fishings from a colony that was microscopically observed to germinate from one of the double contoured conidia like those originally observed in scrapings, and which at no time came in contact with other colonies of any sort (Fig. 6). Descriptions are from growths on mediums and contained strictly according to Sabouraud's formulas, but from ingredients of American manufacture.

Naked Eye Appearance.—Growth was visible within twenty-four hours on all the mediums above named. In the recently isolated cultures the colony was not distinctive until the fifth day, when it became coco-brown. Color developed a little more quickly (on the third or fourth day) after repeated subculture.

In the meantime it was grayish-white and delicately fuzzy. The distinctive brown color developed more rapidly when there was a thin

layer of medium, as in the Petri dishes—even when drying out was prevented by hermetically sealing. The deepest shade of brown, which was about that of an unsweetened dry coco, developed (and most speedily) on glucose agar. The margin was regular, and while definite, was not sharp (Fig. 7).

Morphology is best studied in the large (potato) tubes recommended by Sabouraud or the duplex Petri dishes devised in this laboratory, by both of which thick strata of medium are made available. A solitary point should be inoculated—not a streak.

In these containers the brown color (and at the same time powdery surface) became barely recognizable in three days on glucose agar, in four on plain and proof agars, in five on conservation, and in six on Petroff's. It became strong in the course of two more days, but

Fig. 6.—Spore of *P. brevicaule* isolated from scrapings, germinated and giving rise to mycelia. The spore is a little too much out of focus to show its double contour.

showed differences in intensity when the colony became fully developed, which required about two weeks. At this time the color on both plain and glucose agar was strong yellowish brown, the latter being slightly more colored than the former. On conservation agar it was a pronounced fawn color, on Petroff's, a dirty blackish brown. On proof agar the colony was dirty brownish gray as long as the medium remained very moist, as at the bottom of the tube. Only as it dried out did it take on the stronger dirty gray brown color. Color extended almost fully to the margin of the colony except on proof agar. On the latter it was variable—occasionally covering the whole surface, but generally important only in the center. Elsewhere it was dirty gray.

Luxuriance also varied on the several mediums. In four days glucose agar colonies were 25 mm. in diameter, a little smaller on

plain, proof and conservation mediums, and but from 10 to 15 mm. on Petroff's. The thickness of the colony was also greatest on glucose agar, leading to the production of radial folds in five days. Similar folds developed on the other mediums when they reached a comparable stage of luxuriance, except for plain agar, on which they never developed. Here the colony was always thin and flat—even when a month old. The folds were never numerous—not more than a dozen —except on proof medium. On this there sometimes were as many as thirty at the end of three weeks, and by this time fissures appeared

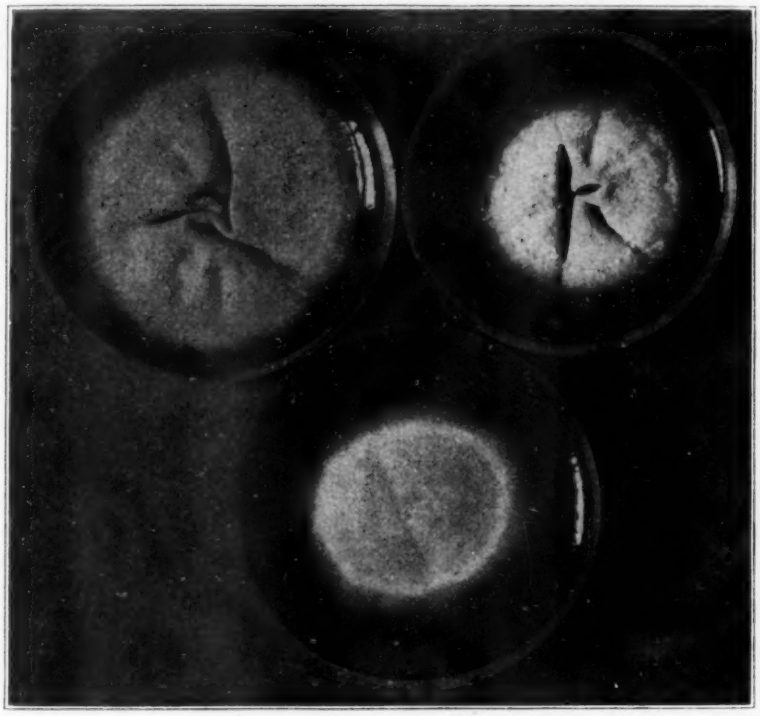

Fig. 7.—Culture full size; upper two on Sabouraud's proof medium; lower on conservation. All are 3 weeks old, planted on a thick stratum of medium and reared identically. Note difference in depth of the furrows, amounting to fissures on the proof medium.

between them—mostly radial—but occasionally transverse near the center of the colony. The depth of these fissures was variable. They were never deep under any circumstances except on proof agar; and became so deep on the latter in four weeks as to separate completely the culture mass and display the medium underneath.

Microscopic Appearance In Hanging Conservation Agar.—In twenty-four hours a conidium was found to have "germinated" and

from it a branched mycelium already extended (Fig. 6). At first colorless, in forty-eight hours the mycelium took on a decided greenish color by transmitted light. As yet no conidia or spores had developed. In sixty-four hours the colony was 8 mm. in diameter. By this time

Fig. 8.—Hanging agar preparation (photomicrograph); growth about 2 weeks old. Earliest spore development at S^1; later at S^2. Typical sporangium in center of illustration. Strings of spores still attached to hyphae—contra Figure 12.

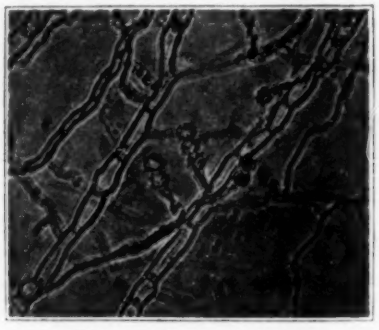

Fig. 9.—Budding of spores in single chain.

intercalated chlamydospores had formed and the ends of some mycelia had become clubbed, suggesting early fuseaux formation. On the fourth day conidia (spores) began to appear. At first they were solitary (Fig. 8), and projected as buds directly from the mycelium both terminally and laterally, but later secondary conidia budded out from

them in a way suggestive of yeasts (Fig. 9). The whole aspect of the colony up to this point was like that of one of those yeasts that develop mycelia in culture.

The buddings continued until on an average a chain of seven or eight conidia had been formed. I have counted up to seventeen. As they multiplied, slender non-segmented hyphae generally developed from the parent mycelium to support them; often the hyphae were thick and segmented. In the earlier colonies there was no grouping of hyphae into penicillium types—these developed only in older colonies, those two or three weeks old. At this stage they extended singly from the parent mycelium like S^1 and S^2 in Figure 8. Conidiophore hyphae

Fig. 10.—Early (terminal) structureless spore budding from neighbor. Note also the jointlike intervals at intersections of some spores.

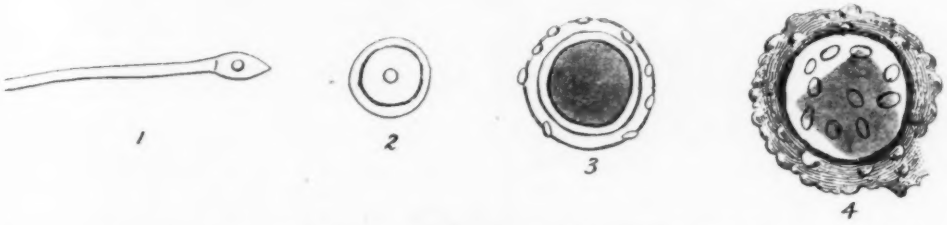

Fig. 11.—Drawing of spores, unstained. All have a greenish cast: 1, very early; 2, later—no granules as yet developed, hyaloid and structureless throughout; 3, beginning development of granules; 4, fully developed spore; granules very coarse; central hyaline part lumpy or distorted. The (ten) ellipsoidal bodies are on the *surface* of the spore, not in its interior.

have the same greenish color by transmitted light that the spores have, and brown by reflected light.

Fully developed conidia measure from 6 to 8 microns in diameter, and young forms from 5 to 6 microns. When the conidium first budded it was a structureless, glassy, greenish spheroid (Fig. 10). As it enlarged a double contour developed and coarse greenish granules appeared on the exterior. The center remained hyaline, however, as determined by careful focusing; although it might appear granular to superficial observation as a result of the overlying and underlying

surface granules (Fig. 11). Stained by methylene blue, the center became strongly blue, while the "shell" and its granules took the color faintly or refused it, i. e., they retained their original greenish cast. Where attached to each other or to the parent hypha, they were often flattened and the double contour disappeared. They were loosely attached to each other, and on this account it was impossible to scrape a chain from the culture medium to a glass slide for photographing, or to obtain an "impression" preparation of them on an albuminized coverslip (Fig. 12). The accompanying photographs, which show chains of conidia, are of living colonies on "hanging agar" preparations. As the colony became older and dried out, the conidia ceased to bud further and became more thickly covered by granules which were much coarser than at first; as a result, the conidia became uniform in size throughout the chain, and comparatively opaque (Figs. 13 and

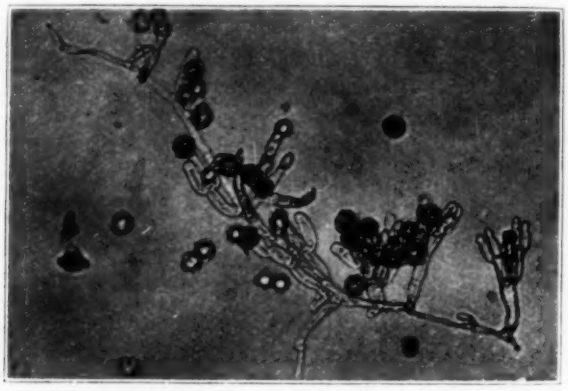

Fig. 12.—Appearance of sporangia scraped from growth; practically all the spores shaken off. Stained with methylene blue. Compare with Figure 2.

14). At the same time, hyphae became branched into typical penicillium form. These were never complicated, generally consisting of seven or eight branches; indeed, frequently these were so widely separated from each other as to require foreknowledge to appreciate that they were really penicillium groups (Figs. 8, 10, 12 and 13). Brumpt recognized the latter indefinite, or lack of, grouping, as indicated in both of his figures, but he does not comment on it. It is important taxonomically.

ANIMAL TESTS

A thick emulsion of spores and mycelia was injected both intravenously and subcutaneously into rabbits (two), guinea-pigs, white rats, white mice and pigeons. No lesions developed, with the exception of foreign body tubercles on the peritoneum; and cultures from heart's blood and peritoneum were sterile eight days after inoculation.

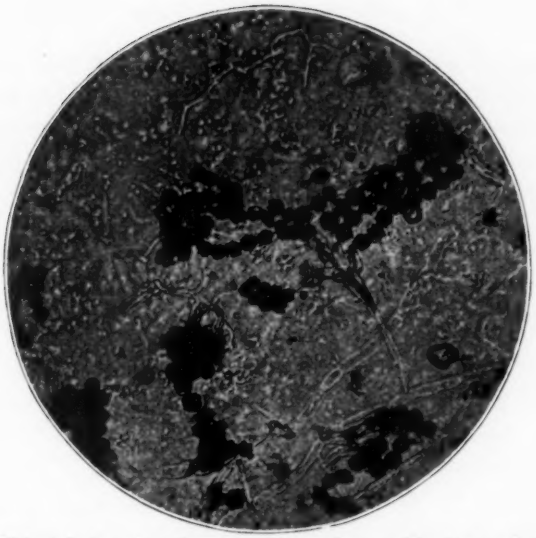

Fig. 13.—Old dried out culture; sporangium with long chains of deeply pigmented spores.

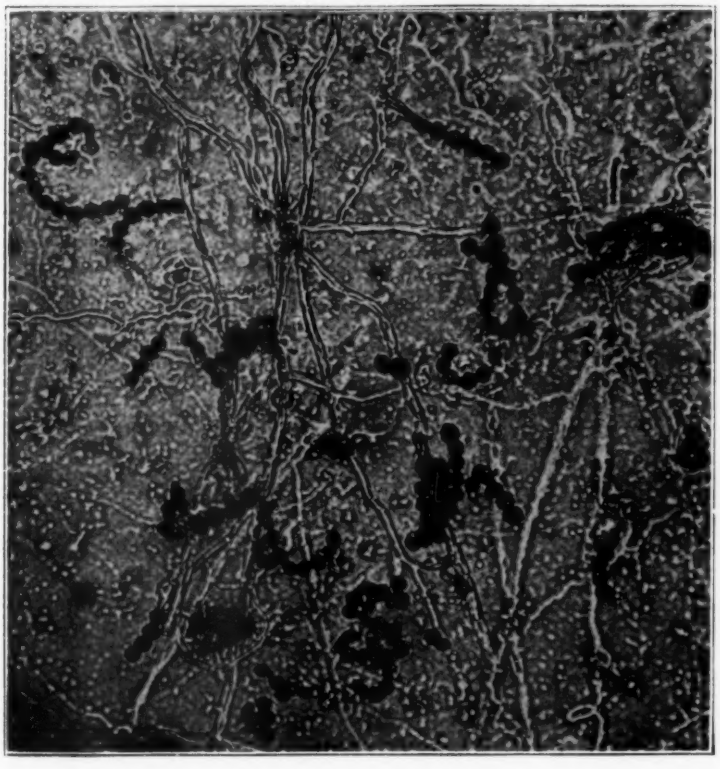

Fig. 14.—Old dried out culture; individual chains of various lengths with deeply pigmented spores. Suggests a monilia in the absence of the typical penicillium corymbs.

Fragments of culture were rubbed under all four great nails of two rhesus monkeys and under the great nails of a human being. No disease developed in any case. In the human case *P. brevicaule* was recovered in culture up to eighteen days after being rubbed in. The next culture was not made until thirty-eight days after inoculation, when it was negative, and has since remained so.

PATHOGENICITY

I cannot claim any pathogenicity for *P. brevicaule*. On the other hand, if limited to my own experience with this one case I would have to reject the idea, not so much on the basis of the negative animal experiments, although these have a certain weight, but mostly because the organism was so inconstantly recovered in cultures, and because so many other organisms were also, and more constantly, found. It will be recalled that Weil and Gaudin also found many different species of fungi in their cases. Why should we single out *P. brevicaule* from the host of others and fasten on it the burden of guilt? But Brumpt's results—five pure cultures in five trials (a remarkable result from such a position as the toe-nail)—cannot be overlooked or dismissed, and therefore it appears to be saner to regard my own results as only modifying our ideas as to its pathogenicity. It will be better to hold our minds open to further light before coming to a final conclusion.

SYSTEMATIC POSITION

There can be no doubt that penicillium groupings are present with this organism—and if the generic diagnosis rests solely on this point, the generic name given it is valid.[3] If, on the other hand, the original genus was based on the presence of these branchings alone and did not include also the individual chains which are present in *P. brevicaule*, there are ample grounds for considering the propriety of indicating a new genus.

The final decision on this point I prefer to leave to the systematist, who can investigate the original type species and compare it with the organism I have studied. Systematists are so constantly renaming and rearranging supraspecific groups that it would be an assumption for any one—biologist, pathologist or dermatologist—to attempt a new name on the basis of a single observation.

As to the specific diagnosis, there is every probability that the organism I have studied is the same as that originally described by

3. Saccardo, D. A.: Sylloge fungorum, Berlin, R. Friedlander & Son, 1886, p. 78.

Saccardo,[4] and figured by him in color.[5] It is certain that it is the same variety as that described by Brumpt and Langeron. The difference between the certainty and probability above implied depends on the difference between Brumpt and Langeron's variety and Saccardo's original one. I have referred to Saccardo's original works and find that his material came from decaying leaves in Italy and that, as figured, the mold (on a plant stem) had a faint brick red color instead of the yellowish brown which appears on our laboratory mediums. Drawings of mycelia, including sporangia, are of the same tint.[6] Otherwise, as far as Saccardo's data are concerned, my organism might be the same as his. It is therefore best to accept Brumpt and Langeron's variety, but in naming it to recognize Saccardo as the originator by prefixing his name and date to Brumpt and Langeron's. *P. brevicaule* is an interesting organism in other respects. First, at an early stage of its growth it shows fructifications like those of monilia and at a later stage those of both monilia and penicillium. Secondly, its conidia agree structurally and tinctorially with those of some monilia (Montoyai). It may thus prove to be a connecting link between the genera monilia and penicillium which may be useful taxonomically.

SUMMARY

A case of ringworm of three toe-nails on two feet is described, in which the scrapings were studied microscopically and cultivated. Mycelia and blastomyces-like spores were found in scrapings, and nine different species of fungi were isolated in cultures. Among the fungi a coco-brown penicillium was isolated, but as it was only cultivated once out of three trials and produced no disease on injection into and inoculation on animals, the author is inclined to question its pathogenicity. This report concerns only *P. brevicaule* and deals particularly with its morphologic and cultural characteristics.

I report the organism for the first time in the United States with a habitat under diseased nails with many other fungi, and add details of its cultural characteristics. I also bring out an important clinical point in that conidia of some fungi resemble and might be mistaken for blastomyces in scrapings.

4. Saccardo, D. A.: Michelia, **2**:547; also in Sylloge fungorum, **4**:84.

5. Saccardo, D. A.: Fungi italici, July, 1877.

6. I have tried to cover this point by growing my strain on both solid and fluid mediums in which decaying leaves were mixed and also on moist and decaying leaves—both sterilized and unsterilized. In no case did I get reddish growth such as Saccardo reported (rubescentia) and figured.

DERMATOBIA HOMINIS *

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With the increasing extension of our commerce into the South American countries it is likely that more and more tropical parasitic diseases will be introduced into the United States. These will be of two types. The first will include only imported cases, in which some factor in the life history will be wanting in northern climates, and the life history of which cannot be completed here. These diseases will, of course, never get a foothold north of Mexico; they will be contracted in the tropics, although in the United States physicians will be called on to diagnose or treat the condition. The second, and far the worst type, will be the diseases for which material and conditions for the completion of their life cycle will be favorable in the United States. These are the most to be dreaded and demand the most careful consideration on the part of health officers, physicians and the public. To the first type of parasitic diseases belongs that condition caused by the larvae of *Dermatobia hominis*.

If the recorded incidence of infection by *Dermatobia hominis* in the United States is to be regarded as evidence, its occurrence must be very infrequent. Ward [1] has published a very excellent monograph on the subject, reviewing all the cases up to that date and definitely showing that the disease known as "ver moyoquil," "ver macaque," "torcel," "muche," "berne," etc., is caused by one species of larva, so that *D. noxialis* and *D. cyaniventris* are synonyms of *D. hominis* (Say).[2] In his collection of cases, he found that the first reported from the United States was by Say,[2] describing the case of Dr. Brick, who contracted the disease while traveling in South America. The second case was reported by Penniston,[3] who removed a larva from a sailor in the Charity Hospital in New Orleans. The sailor had acquired the parasite while traveling in Vera Cruz and Tabasco, Mexico. Matas [4] reported the third case, that of an Englishman from Spanish Honduras.

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* From the Section on Clinical Laboratories, Mayo Clinic.

1. Ward, H. B.: On the Development of Dermatobia hominis, Mark Anniversary Volume, Article xxv, 1903, pp. 483-512.

2. Say, T.: On a South American Species of Oestrus which Inhabits the Human Subjects, New Orleans M. & S. J., 1844, p. 23.

3. Penniston, T.: A Case of Malis Oestri, or Gadfly Bite, Occurring in Human Subjects, New Orleans M. & S. J., 1844, p. 24.

4. Matas, R.: Report of the Case of a Patient from whose Subcutaneous Tissue Three Larvae of a Species of Dermatobia were Removed, with Remarks, New Orleans M. & S. J., **15**: 161, 1887.

who was operated on in New Orleans, three larvae being removed from the gluteal region. In this paper he refers to a previous case, that of a Frenchman, also from Honduras, in the Charity Hospital. Blanchard [5] refers to three or four cases from America; they were, however, reported to him in the form of personal communications. These are all that had been recorded up to 1903, and I have been able to find but four in the American literature since that time.

One is reported by Brooks [6] in 1905. The patient had been in Panama and in good health. Six weeks before presenting himself for examination he noticed three small lumps, one in the groin, one on the flexor surface of the forearm and the third over the left shoulder. Each tumor showed at its apex "a small perforation through which a small, moving, black body could be made out." There was a great deal of local pain and a slight rise of temperature. The tumors were opened and the "worms" squeezed out. The largest was 2 cm. long and 9 mm. in breadth. The wounds healed rapidly. There was a marked increase of eosinophils in the blood.

In discussing the case, Dr. James Ewing said that Dr. Alexander Lambert had sent a similar parasite to the Cornell Laboratory which had been removed from a patient, who had recently come from Panama.

A second case was reported by Costa.[7] He was asked to see a child who was returning on a boat from Tiberiza to Brazil. The child had been living for ten months in the former place and had recently developed three tumors on her head. These were roundish and of "the size of a small mandarin." Costa expressed from each a larva of Dermatobia. While the case was reported in a North American journal, it is quite evident that this is not in any sense a North American case.

The third case, reported by Singleton,[8] is that of a German who had lived for six months as a tramp in Mexico. He presented himself to a physician in Galveston, Texas, with a tumor on the dorsum of the penis just behind the glans. The swelling was "as large as a pecan," felt hard and was only slightly inflamed. It felt more like scar tissue than anything else, and a little pus and serum exuded from a central depression. The patient said that flies were very common

5. Blanchard, R.: Contributions a l'etude des dipteres parasites, Ann. Soc. entomol., **65**: 641, 1897.

6. Brooks, H.: A Case of Dermatobia Noxialis, with Demonstration of Larva, Med. News, New York **86**:430, 1905.

7. Costa, E.: Two Important Parasites of the Skin, J. Cutan. Dis. **28**:24-32, 1910.

8. Singleton, A. O.: Report of a Case of Dermatobia Noxialis in Man, J. A. M. A. **58**:1282 (April 27) 1912.

in parts of Mexico where he had traveled and that he had been bitten on the penis while bathing. From the center of the mass Singleton extracted a larva of Dermatobia about three fourths of an inch long.

The last case, reported by Dunn,[9] was that of Dr. Clark, who became infected while making a tour by way of the Boqueron River in the interior of Panama. He noted on returning to camp that he was acting as a host for a certain species of tick, and later at the site of the tick bites developed inflamed wounds, exuding serum. In each was found a larva of *Dermatobia hominis*. A few months later while huntng near Arraijan on the west side of the canal he became infected a second time, a tick attaching itself to the right side of the abdomen. About three weeks afterward, he removed a larva of *D. hominis* 2 mm. in length, from the point of the tick bite. This incidence is offered by Dunn to demonstrate that the tick of the species *Amblyomma cajennense* is capable in some way of acting as a carrier for the eggs, and is "also instrumental in assisting the larva to penetrate the skin." This is interesting and should be further investigated, since practically all authors have believed the parasite requires some species of mosquito as a vector during its life cycle.

I am deeply indebted to Dr. A. E. Mahle of the Mayo Clinic for turning over to me a larva of *Dermatobia hominis* which had been sent to him by Dr. Donna M. Parker of Peoria, Ill. This had been extracted from a patient whose history is presented herewith.

REPORT OF A CASE

Mr. W. F. H., aged 28, of Jacksonville, Ill., had been in the tropics from June to September, 1917, from January to July, 1918, from March to September, 1919, and from December, 1919, to March, 1920. Except for occasional headaches and one attack of malaria, he had been in good health. He had been in Panama about one week when he noticed a local sensation in his shoulder like a sharp pin prick. Five or six days later, a rather painful boil appeared which several days later appeared to be a carbuncle. He applied cataplasm of kaolin; the mass came to a head and a physician lanced it and removed a "worm" and a quantity of yellow pus and dark blood. Later the patient himself extracted a worm from another site. He had been in the United States a short time when he had other abscesses. Dr. Parker opened these, removed the larvae and packed the opening with phenolated gauze. The patient says the treatment was entirely satisfactory and that he has had no further trouble.

DESCRIPTION OF PARASITE

The worm which the patient himself extracted is shown in Figure 1 and is enlarged about three times the normal size. Actually it is 9 mm. long and 3 mm. wide at its greatest diameter. It is

9. Dunn, L. H.: The Tick as a Possible Agent in the Collocation of the Eggs of Dermatobia Hominis, J. Parasitology **4**: 154, 1918.

white, and the rows of black hooks stand out sharply. The anterior portion is about 3 mm. long, the posterior 6 mm. I can agree with Ward in his description of the arrangement of the hooks. The first, second and third somites bear each a row of small hooks; the first has the smallest. The fourth somite has a complete row of hooks anteriorly with a row of larger ones posteriorly, interrupted ventrally. The fifth and sixth segments have anterior complete and posterior incomplete rows of hooks, while the seventh has only an anterior complete row. The body tapers posteriorly from the last row of hooks, until it is about half a millimeter in diameter. The terminal portion of the larva is inrolled and the exact nature cannot be described.

The tenth somite is in the form of a collar and is covered with minute hooks. These are not black, like the hooks of the anterior somites, but are reddish brown. The last somite is retracted into the

Fig. 1.—Larva of Dermatobia hominis: *A*, dorsal view; *B*, ventral view.

collar formed by the tenth. The first bears the two mammiform protuberances on the dorsal surface described by Ward and the single pair of mouth parts which consist of conspicuous heavy black hooks bent in a ventral and posterior direction. Minute description of the hooks and somites is omitted, for it would be merely a repetition of the excellent description of Larva A given by Ward, which was of about the same size as the one I studied.

GEOGRAPHIC DISTRIBUTION OF THE PARASITE

The distribution of the parasite is as follows: Brazil, to 18 degrees south latitude and west to the mountains, French and British Guiana, Venezuela and the Island of Trinidad, Colombia and Peru. Records are found of its occurrence in Costa Rica, Honduras, Guatemala and certain Mexican states. It occurs westward of the great mountains on the Pacific coast. It does not appear on the great central plateau of which the altitude is excessive and the mean temperature insufficient.

Figure 2

Figure 3

Fig. 2.—Young larva of Dermatobia hominis, × 3. (After Castellani and Chalmers.)

Fig. 3.—Older larva of Dermatobia hominis Macquart, × 2½. (After Castellani and Chalmers.)

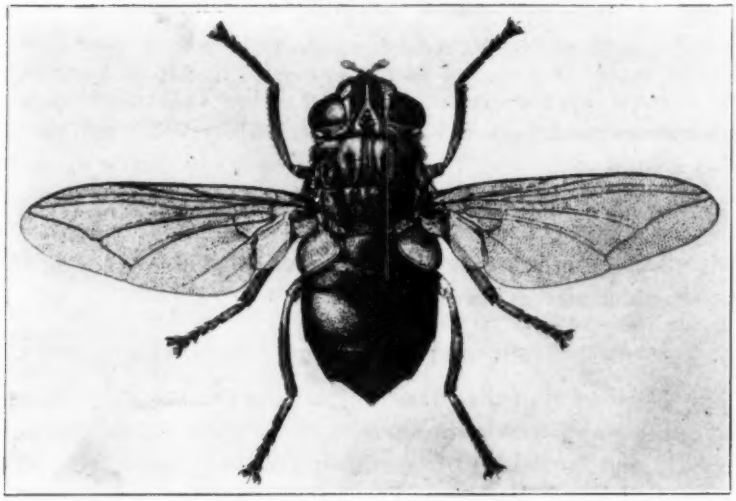

Fig. 4.—Dermatobia hominis Macquart, × 3. (After Castellani and Chalmers).

It is interesting to note that while it does occur very close to the southwestern border of the United States, no cases have been reported in which the disease has been contracted within this country. Blanchard tried to locate incidences of the infection by extensive correspondence with societies and individuals in Texas and Louisiana, but failed.

The larvae have been found in the flesh of many different kinds of animals, including cattle, pigs, dogs, mules, agouti, jaguars, monkeys, toucans, ant-thrushes and man.

There is still much work to be done on the life history and mode of transmission of the parasite. The natives of many of the countries in which the infection is found call the larvae mosquito worms and think that a mosquito of the genus Psorophora is responsible for the infection. Surcouf has found these fly larvae cemented to the mosquitoes of the genus Janthinosoma, a very vicious biter. It is possible that the young larva escapes from the mosquito as it bites, and takes up its habitat in the skin of the victim. The young larva is at first club-shaped and is then known as "ver macaque." Later it becomes worm shaped and is known as "torcel" or "berne." The larva described above is older than a ver macaque but not yet developed to the stage of the torcel (Figs. 2 and 3). If not interfered with, it remains in the skin until an abscess forms and the larva is thrown out, drops to the ground, pupates, and finally develops into the imago. The adult fly is shown in Figure 4, and is known as a "gadfly." Typically the larva causes local pain and itching, with swelling, and edema of the surrounding region, "giving rise to a boillike swelling, rather hard, of a deep red color, with a central opening." Here one sees at times the stigmas of the organism, and it may appear or disappear like a jack-in-the-box. The Brazilians try to kill the larvae with tobacco smoke, or apply fat to the opening to cause asphyxiation. They are easily extracted with sterile forceps, the wound opening enlarged and the swelling treated in essential respects as a furuncle. By the last method recovery is usually rapid and satisfactory.

ANAPHYLACTOID DERMATITIS DUE TO DIRECT CONTACT WITH ANIMAL EPIDERMAL STRUCTURES *

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In a recent paper dealing with certain cutaneous manifestations of anaphylaxis, a well known writer [1] states that "the cutaneous phenomena which occur as a result of the absorption of foreign proteins through the respiratory tract and possibly through the skin itself have not received the attention and study that they deserve." This statement, combined with a recent illuminating experience of my own, has prompted the presentation of this brief paper on a phase of this subject which is, I believe, of definite clinical interest, namely, that the skin alone, and even limited areas of the skin, may be sensitized by and react to direct contact with specific substances contained in the epidermal structures of certain animals, as shown in the following case report.

REPORT OF A CASE

History.—Mrs. R., aged 39, an office assistant, came under observation Feb. 2, 1919, presenting a skin eruption of six months' duration, during which time she had been under constant treatment. Her previous history was irrelevant and she made no complaint aside from the skin disorder.

Examination.—This revealed an erythematous and papular eruption involving practically the whole of the face, neck and chest, the anterior surfaces of the forearms and the cubital spaces; the hair was harsh and dry, the scalp scaly but not actively inflamed. There was considerable swelling about the eyes and areas of weeping surface over the lids and at the angles of the nose. Itching was intense, particularly at night, and the duration of the condition had induced marked nervous disturbance.

Treatment and Course.—The distribution of the eruption and the appearance of the scalp suggested a seborrheic dermatitis and treatment was begun with that diagnosis. Some evidence of digestive disturbance led to careful regulation of the diet, which, with mild local applications, brought about prompt improvement; this was, however, only temporary. About March 1 an examination of the mouth disclosed a number of alveolar abscesses and definite pyorrhea for which she was placed under the care of a competent dentist; this also resulted in temporary improvement. During the succeeding few months repeated inquiry was made as to a possible external source of irritation—plants, chemicals, etc.—but none could be discovered, and on June 1, nearly one year after the beginning of her difficulty, her condition was worse than ever, notwith-

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* Read at the Forty-Third Annual Meeting of the American Dermatological Association, Asheville, N. C., April, 1920.

1. Sutton, R. L.: Ragweed Dermatitis, J. A. M. A. **73**:1433 (Nov. 8) 1919.

standing constant efforts to determine the cause of the disorder and to relieve it by treatment. A gastro-enterologist was then consulted, who discovered an absolute achlorhydria, and she was put on strict diet again with seeming benefit. Another internist discovered a chronically inflamed appendix, and this was removed on Sept. 1, 1919. During her stay in the hospital the skin cleared up completely and it was believed that relief was permanent; on her return home, however, the eruption recurred with increasing violence. The patient was now reduced almost to desperation and was frequently unable to attend to her work. Relief came unexpectedly through her own discovery that the skin always became immediately worse after cleaning out the pen of a guinea-pig belonging to her small son and allowing it to run about over her shoulders. Disposal of the animal was followed by prompt and permanent disappearance of the eruption and complete clearing of the skin, and now, eight months later, there has been no recurrence.

Tests to Determine Specificity of Reaction.—After discovery of the cause of this eruption and its complete disappearance, numerous tests were made to determine the actual specificity of the reaction, this being done by binding firmly on the skin patches of animal hair and leaving them for definite periods. The first test made with guinea-pig hair applied to the side of the neck for four hours gave a strongly positive result with local vesication and an erythematous eruption, which within twenty-four hours had spread over the front of the chest, the chin and lower part of the face on the same side, subsiding in about three days. Repetition of this test on various parts of the body soon showed that the skin never involved in the original eruption always gave a negative result, even after six hours' application, while the skin of areas previously affected gave a positive result after two hours' application of guinea-pig hair. Control tests made in each instance on another person, and similar tests made with hair of other animals—cat, dog and horse—were all uniformly negative, the last series being completed on April 10, with a final positive result.

SKIN SENSITIZATION

In so far as this case may be accepted, it seems to prove that circumscribed areas of the skin may be sensitized by and react to direct contact with substances which are without effect on the normal skin. This is, of course, not an original observation, von Pirquet [2] in his early work having noted that the skin of his left arm, which he habitually used for experiments, was sensitive to a tuberculin dilution of 1:1,000 while the skin of his right arm was negative to tuberculin ten times as concentrated.

Hay fever, too, is regarded by some observers [3] as a definitely localized sensitization of the epithelium of certain mucous surfaces, reaction occurring only on direct contact with the sensitizing agent, and further that desensitization can be accomplished only by local application of a specific vaccine.

The manifestations of cutaneous hypersensitiveness, as ordinarily observed, consist of hyperemic and urticarial eruptions of general dis-

2. Zinsser: Infection and Resistance, New York, Macmillan Co., p. 445.
3. Zinsser: Infection and Resistance, New York, Macmillan Co., p. 437.

tribution and relatively low grade activity, resulting from the action on the cutaneous tissues of specific substances carried by the circulating fluids in necessarily minute amounts. Such reactions, however, induced by local application of the sensitizing agent, are more violent because of the greater concentration of the antigen, and it is probable that in the cases of rag-weed dermatitis reported by Sutton [1] and Hannah,[4] the acute inflammation of the skin was due to direct contact with pollen, even though sensitization resulted from absorption through the respiratory tract. Similar instances are frequently observed, such as attacks of asthma or hay fever following close proximity to certain animals, with coincident development of acute dermatitis on areas of the skin brought into direct contact with the animals.

SKIN SENSITIZATION AND ANAPLYLAXIS

The relation of skin sensitization to the more general condition known as the "anaphylactic state" is at present not clear. Since it is well known that the skin may be sensitized by many substances non-protein in character, the resulting cutaneous phenomena are held by many observers not to be true manifestations of anaphylaxis. It has been definitely shown, in a recent paper by Fleischner [5] and others, that the highest degree of anaphylaxis may be induced without the coincident production of cutaneous hypersensitiveness. It is possible, therefore, that such phenomena are not antigen-antibody reactions, but purely skin responses to stimuli rather of the nature of toxins, yet their definitely specific character so closely resembles that of anaphylactic reactions as to justify the application to them of the term anaphylactoid.

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4. Hannah, L.: Ragweed Dermatitis, J. A. M. A. **72**:853 (March 22) 1919.

5. Fleischner, E. C.; Meyer, K. F., and Shaw, E. B.: A Résumé of Some Experimental Studies on Cutaneous Hypersensitiveness, Am. J. Dis. Child. **18**:577 (Dec.) 1919.

SO-CALLED DERMATITIS DYSMENORRHEICA

REPORT OF A CASE, WITH REVIEW OF THE LITERATURE

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Ever since the publication of the article by Matzenauer and Polland [1] dealing with a peculiar dermatosis occurring in women having dysmenorrhea and manifesting itself during the menstrual periods, there has been much controversy among dermatologists with regard to the *genuineness* of this affection. The authors describe what they consider to be an entirely new entity. Similar cases had been previously observed and recorded, but they were classified under the hysterical dermatoses, dermatitis artefacta, malingering, etc., that is, the self-inflicted dermatoses. A detailed description of five cases of the new disease is given.

One of these was the subject of a careful study made by Kreibich [2] antedating the observations of Matzenauer and Polland. Kreibich believed that the disease manifestations were due to a reflex neurosis, provoked by increased irritability of the dominating vasodilator center. His studies led him to advance the theory of a so-called angioneurotic inflammation.

On the basis of their studies, Matzenauer and Polland offered a totally different interpretation of the pathologic processes involved in the causation of this peculiar dermatosis. All of the patients were women afflicted more or less with dysmenorrhea. The eruptions consisted of spontaneous, usually symmetrical lesions affecting the face, trunk and extremities, occurring in the form of erythematous patches, urticarial wheals, but more often, vesicular eruptions resembling ordinary weeping dermatitis. Some of these lesions underwent spontaneous necrosis. In some of the patients, the necrotic efflorescences were distinctly linear in configuration, clinically indistinguishable from the linear self-inflicted injuries of malingerers. Other lesions were strikingly limited to the follicular appendages of the skin. A goodly number of pages in this long article are devoted by the authors solely to the demonstration of the fact that these apparently artificial and self-inflicted formations are in reality *spontaneous* in nature. Physical

1. Matzenauer, M., and Polland, R.: Dermatitis Symmetrica Dysmenorrheica (A Contribution to the Angioneurosis Question), Arch. f. Dermat. u. Syph. **111**:385, 1912.

2. Kreibich, C.: Die Angioneurotische Entzuendung, Vienna, M. Perles, 1905; Die Angioneurosen und die haematogenen Hautentzuendungen, Arch. f. Dermat. u. Syph. **95**:405, 1909.

examination of some of the patients revealed the coincident occurrence of cardiac vasomotor disturbances, circulatory abnormalities and psychoses. Taking into consideration the hysterical element, and realizing the difficulties in the handling of this class of patients, the authors describe with the greatest precision the various precautions which they took to rule out every possibility of malingering. Among these was, of course, the guarding against self-inflicted injuries by means of stable and impervious bandages, etc. In one of the patients, the beginning of a lesion and its subsequent developmental stages were observed by one of the physicians, while the subject was fast asleep. Another woman visited the clinic just before a new patch began to appear on the skin, affording an opportunity to watch its progress and gradual development. Every possible bit of evidence is submitted by the authors to prove their contention that malingering plays no part in the pathogenesis of the different eruptions which they describe. It is their belief that the dermatosis is an expression of systemic disease, possibly the result of toxic metabolic products, due to derangement of the ovarian follicles.

Many excellent photographs accompany the article. These demonstrate all the different types of lesions described in the text: erythematous, urticarial, follicular, bullous, hemorrhagic, necrotic, etc., but above all, they illustrate with exceptional vividness pronounced lesions of *linear configuration* which, even to the inexperienced eye, seem to call loudly for the label "dermatitis artefacta." The dubiousness with which the entire contribution is regarded by many dermatologists may unhesitatingly be attributed to the actual, vivid portrayal of the linear formations accompanying the text. Those who regard the illustrations alone and decide to digest the lengthy text at some future and perhaps more auspicious time, instantly arrive at the conclusion that the illustrations represent the vagaries of hysterical women who purposely or unconsciously inflict various injuries on their skins. On the other hand, there are those who, not content with a view of the illustrations alone, suffer themselves to read the text as well. Be it said of these that the majority are by no means diverted from their prejudice in favor of an artificial eruption. To quote one eminent authority, to wit, Hartzell:

> Very recently Matzenauer and Polland, under the name dermatitis symmetrica dysmenorrheica, have reported a number of cases, occurring for the most part in young girls, characterized by linear patches of erythema and excoriations, wheallike lesions and exceptionally by superficial necrosis of the skin. A study of the history of these cases, and more especially of the excellent illustrations which accompany the report, leaves but little doubt in the author's mind that the eruptions were factitious.

Criticisms by other observers will be referred to later, more in detail.

In justice to Matzenauer and Polland's painstaking work, and in view of the fact that they state without equivocation that the lesions, despite their great resemblance to artefacts, are in reality spontaneous, it is only fair for us to devote some space to the consideration of the arguments, pro and con, which the authors submit in favor of their contentions. Taking the bull by the horns, they state in the very beginning of their article that in the earlier period of their studies they regarded with much skepticism the prevailing views entertained about the etiology of various angioneurotic cutaneous manifestations, and more especially with reference to the etiologic factors obtaining in the class of cases forming the subject of their report. They paid particular attention to the question of malingering, feigned eruptions, hysterical manifestations, etc. As a result of their studies they concluded that they were dealing with an "idiopathic, hitherto little known and insufficiently described disease, which in every respect presented a characteristic, typical course, and whose segregation (from other dermatoses) was justified on the strength of its probable etiology." As already stated, they included in their group of five patients one of Kreibich's "angioneurotic" cases; emphasis is laid on the statement that none of the other cases described by Kreibich is included under the category of dermatitis dysmenorrheica. The latter is to be strictly differentiated, not only from the angioneuroses of Kreibich, but also from all the different affections described in the literature under such captions as hysterical, neurotic, angioneurotic gangrene, spontaneous gangrene of the skin, zoster hystericus, herpes neuroticus, etc. In other words, they contend that they are dealing with a disease entity.

A detailed account of the authors' five cases makes interesting reading, but is too intricate to be recapitulated here. They draw a composite picture of the disease somewhat as follows:

A PICTURE OF THE DISEASE

The first thing the patient feels in the affected region of the skin is a burning sensation; all patients tell the same story. The intensity of the sensation varies greatly; often they are not even conscious of the burning, especially if the lesion begins during sleep, which often happens; at other times the sensation may be intense and prolonged. Coincident with this subjective symptom, the affected area presents an urticaria-like swelling, of a faint rose-red or pale eosin color, and the size of the fully developed lesion. The lesion is often more readily felt than seen. At times the original spot shows a peripheral zone of spreading erythema, while the central portion assumes a

more marked urticarial aspect. The very faint, pale red tinge of the lesion differentiates it strongly from the more intensive scarlet redness of other inflammatory processes, such as traumatic or bacterial inflammations.

After a short while, from a quarter to a half hour, a further stage of development manifests itself: The follicular orifices stand out more distinctly, each one being surrounded by a very narrow anemic zone, simulating a perifollicular urticaria porcellanea; this appearance is soon followed—especially in the slowly progressing cases—by an exudation of serum into the funnel-shaped follicular orifice which it soon fills; subsequently a thin, yellowish-brown crust forms. All these manifestations are always strictly limited to the follicles. Later on, especially in cases running a more acute course, a superficial desquamation about the follicles ensues, leaving a vesicular zone around each orifice. The follicles being close together, these vesicular areas soon coalesce to form patches of weeping dermatitis or yellow crust-covered lesions, simulating traumatic excoriations. Some of these weeping patches have little zones of fine vesicles.

This process always runs its course within a few hours, acquiring its maximum of development in that time, resulting in the production of a lesion which is red and inflamed, weeping and partly covered with serofibrinous crusts. Owing to the diffuse edema, the patch is slightly elevated and is surrounded by a more or less well marked zone of erythema. The crusts are often brown, due to minute blood extravasations. The formation of the latter may be readily observed at the edge of a lesion, contiguous to the unaffected skin, where the perifollicular edema makes the follicular orifices much more prominent. The extravasations visibly take place about and into the mouths of the follicles. The filling of a dilated follicular orifice with a tiny drop of blood is sometimes actually observed with the naked eye. If the process of development is slow, the lesion appears merely as a patch of punctate follicular extravasations; if acute, there is a central weeping area, with a zone of these follicular formations.

The further manifestations are either of secondary nature or are the result of involution of the lesion. External influences, such as rubbing or scratching, may result in superficial excoriations or slight hemorrhages, thus intensifying the inflammatory process, causing increased exudation and crust formation. Thus the lesion may assume the appearance of a rather deep-seated excoriation. Usually the necrosis and the detachment of the epidermis reaches no farther than the rete malpighii; occasionally the process extends down to the papillary body, usually as a result of external injury. As a rule, healing occurs beneath the crusts within three or four days; but for some time after,

the area presents a reddish spot, which later becomes brown, that is, distinctly pigmented. The same areas may, however, be affected in repeated attacks without leaving any traces.

In the more severe cases, the necrosis may extend deeply, resulting in the formation of hypertrophic scars and keloids. In these cases, a dry necrosis appears from the start, instead of a weeping surface. There is an anemic infarct, which at first is pale, later becoming distinctly brown from the blood pigment; the process of involution of these lesions, extending deeply into the corium or to the subcutaneous fat, is extremely slow, and is associated with a purulent exudate surrounding the necrotic mass.

As to the localization of the patches, any part of the body may be affected; the face is the area of predilection, the next most often affected parts being the hands, the trunk and the upper and lower extremities. In one of the patients, there was a coincident eruption on the tongue and buccal mucosae. The lesions are almost always symmetrical in distribution; they are usually round or oval on the cheeks and buttocks, while on the extremities they are linear in outline.

CAUSATION OF LESIONS

The question now arises, are these lesions spontaneous in nature or are they self-inflicted?

A series of experiments was carried out in Case 1, this patient being the same one whose case was reported by Kreibich as Case 4 among the "angioneurotic inflammations." Kreibich did not interpret the lesions as being a menstrual dermatosis associated with dysmenorrhea; he merely cited the case as one example of angioneurotic inflammatory dermatoses. Even at that, the great majority of dermatologists refused to believe Kreibich's statement that the lesions were anything but self-inflicted, much to that author's chagrin. At all events, Polland had this patient under his personal observation, not only during the period of Kreibich's supervision, but also for an entire year thereafter. In the course of that year, Polland had ample opportunity to satisfy his curiosity with regard to the question of malingering.

The lesions appeared under impervious dressings of "zinc-lime," so applied that it was impossible for the patient to practice deceit.

On one occasion, a lesion appeared at a certain time on the right leg. The analogous (unaffected) area on the left leg was immediaetly encased in an impervious dressing and the patient was kept constantly under the physician's surveillance thereafter. Two hours later the dressing was removed, revealing a patch identical in appearance with that on the right leg.

The entire trunk was encased in a sort of cuirasse of impervious bandages before the patient retired. On removal of the covering in the morning, lesions were found where they had previously been absent.

The patient was constantly under the watchful eyes of other patients, nurses, visitors and physicians. In one of the patients suspected of being a malingerer, not only was a strict surveillance carried out day and night, but a special nurse was employed to accompany the patient even to the toilet, and every conceivable article with which artificial lesions might be produced was kept beyond the reach of the girl.

On one occasion, a large watch crystal was applied by means of adhesive tape over a beginning erythematous patch; one of the physicians watched this patch constantly, and observed the development of the lesion as it progressed to a vesicular dermatitis.

Numerous other tests of similar character were carried out. But according to the authors, the results of these tests, convincing as they seemed to be, were in reality only negative in character. They determined to furnish positive proofs relative to the spontaneity of the eruptions.

Thus, a patient (Case 2) was observed presenting a very faintly outlined erythematous patch of skin over the region of the left kidney, of only a few minutes' duration. The lesion was watched unremittingly by a physician during the subsequent two hours. In that period of time, the patch underwent the various cyclical changes described before, terminating in a weeping dermatitis, directly under the observer's eye. When the erythema was first visible, there was absolutely no trace of epidermal changes on the surface, as would have been the case had the lesion been provoked by some artificial means.

In another patient (Case 4), the girl complained of a burning sensation over the sternum, of only a few minutes' duration. On examination, the area was found to present nothing but a faint prominence of the follicular orifices in a small spot, circular in outline. This was incessantly kept under observation, the patient stating that she felt confident that a lesion was about to develop there. A little later, the follicular orifices became markedly enlarged, a perifollicular edema supervened, followed by the usual little urticarial zone surrounding each orifice. The next phase was manifested by a serous exudation within the follicles, then an extravasation of tiny drops of blood, which ended in crust formation. There was no evidence of dermographia. At the beginning of the process, the epidermis was absolutely intact.

Many experiments were carried out to provoke lesions by artificial means, in an attempt to produce lesions simulating those exhibited by the patients. Control tests were also made. Among the methods

employed were the use of a stiff-bristled nail brush, applications of ethyl chlorid, irritation by means of faradic electricity and many other irritating agents. All these experiments proved negative.

In all five patients there were associated manifestations of menstrual disorders: irregularity, scanty flow, amenorrhea, dysmenorrhea.

HISTOPATHOLOGY

For microscopic examination, the authors excised part of a necrotic lesion from the forearm. The pathologic process seemed to originate in the capillaries and deep vessels of the skin. The large and small blood vessels were greatly dilated and were surrounded by a dense round cell infiltrate. This infiltrate followed the branching vessels to their finest divisions, including the most superficial capillaries. The latter also were dilated, engorged with blood and surrounded by round cell infiltrates, some of them obliterated. These vessels were especially evident in areas underlying small epidermal vesicles. The sebaceous glands and hair follicles were surrounded by dilated and inflamed vessels; but the sebaceous and coil glands themselves were unaffected. The most pronounced changes were found about the follicles. The deeper portions were surrounded by a net of dilated and inflamed vessels; the branches of these vessels could be readily traced, with their dense perivascular infiltrates, to the subepithelial layer of the skin.

Surrounding the follicular orifices, the epidermis was raised by the exudate and under it was a layer of blood and fibrin. The little necrotic area was enclosed in a vesicle "membrane" (Blasenwall), toward which dilated vessels, surrounded by inflammatory infiltrates, were seen coursing. The small cutaneous nerves exhibited no signs of inflammation or other changes.

The histopathologic picture gives the impression that the pathologic process originates primarily in the blood vessels; the inflamed and thrombotic vessels give rise to exudation, the formation of vesicles, and eventually necrosis. It may be safely assumed that the inciting agent of the dermatosis lies in the blood vessels—an assumption favoring the so-called "hematogenous inflammatory theory."

In their concluding paragraphs, Matzenauer and Polland state:

> Our dermatosis is characterized by peculiar, spontaneous inflammatory manifestations, usually appearing symmetrically, in chronic successive crops; the lesions are partly erythematous, partly urticarial in nature, most often, however, appearing in the form of a weeping dermatitis; more rarely, as spontaneous necroses of the skin. Coincident with the disease, there are frequently vasomotor disturbances of the heart and circulatory organs, and sometimes also, psychic manifestations.

These changes appeared only in women suffering from dysmenorrhea, and are based on a constitutional affection, most probably invoked by toxic metabolic products, due to malfunction of the ovarian follicles.

REPORT OF A CASE

The patient whose history is here recorded gave a personal history and exhibited lesions that seemed to conform in almost every important detail with Matzenauer and Polland's description of dermatitis dysmenorrheica. She was presented before the New York Dermatological Society, May 25, 1920. At that time, the patient had been under our observation only a short time and the presentation was accordingly brief. Furthermore, the lesions that she exhibited on the day of the meeting were in the final stage of evolution, consisting of little more than a moderately inflamed area of yellowish skin on the left cheek, which gave the appearance of having been bruised. Following the presentation of the patient, the discussion of the members brought out the fact that the majority looked on the lesion as being of artificial character—most likely self-inflicted. After the total subsidence of the lesions then present, we had the opportunity of observing the patient for a period of time embracing two successive menstrual cycles, during which new eruptions appeared, permitting careful study of their involution and evolution.

History.—Mrs. H. B., aged 30, married, of Russian birth, referred to us by Dr. Elihu Katz of this city, a resident of Bangor, Me., complained of a recurrent eruption on the face and chest, the duration of which was one and a half years. The father was living and well, except for occasional "heart and lung trouble." The mother was living and well. Three brothers were dead; the first and second brothers were born before her, the first was possibly still-born, and the second lived two days after birth; the third, two years younger than she, died of pneumonia at the age of 28. Two sisters died in infancy before she was born. One sister, six years older, now living, had "kidney and bladder trouble." Her paternal grandfather was asthmatic and had been in bed four years with "rheumatism." Her paternal grandmother had "stomach trouble." The maternal grandfather died nine years before of cancer. The maternal grandmother had been paralyzed and bedridden for four years, and had kidney disease with edema. There was, then, history of heart trouble in the father; no tuberculosis in the family; kidney trouble in the maternal grandmother; no epilepsy, insanity or nervous derangement; cancer only in the maternal grandfather and no history of skin diseases in the family.

The patient had had measles, mumps and scarlet fever in childhood and a severe attack of typhoid fever at the age of 9. Tonsillitis appeared every winter. There was no history of "rheumatism." She had had influenza-pneumonia two years before, complicated with pregnancy. She underwent an abdominal operation five years before, but did not know its nature. The left tympanic membrane had been lanced three and a half years before for otitis media. She had been married eleven years; her husband was living and

well. She had had four children; the first two were living and well, the third was still-born at 7 months, the fourth died of pneumonia at 8 weeks. The last pregnancy was in the winter of 1919.

She had had frequent supra-orbital headaches, of migrainous type, associated with attacks of vomiting, during the last nine years. Eye-glasses fitted by a physician did not help these headaches. She had had frequent tinnitus in the left ear since the attack of influenza. There was no muscae volitantes. There was no history of "nervousness," poor memory, hysteria, etc. She heard well with both ears, but had an intermittent left aural discharge since the attack of otitis. There was no history of trouble with vision, but on account of headaches, she had glasses fitted nine years before. There was no history

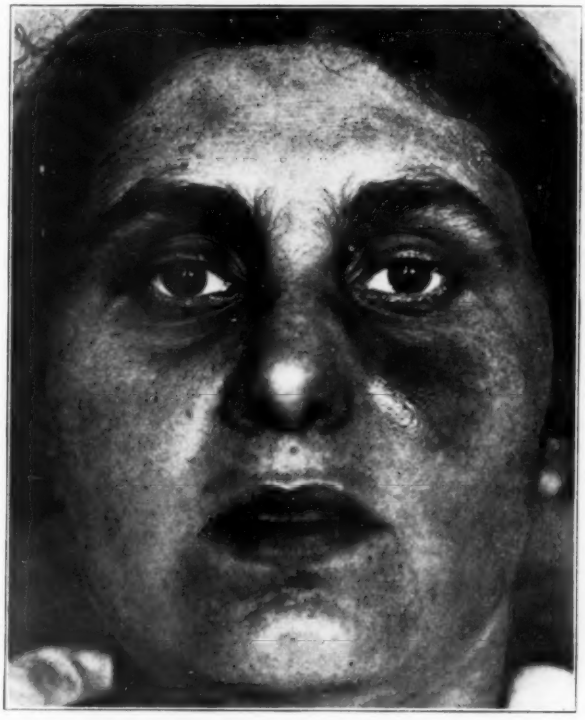

Fig. 1.—Patient on the third day of the menstrual period, showing circumscribed patch of erythema with beginning vesicle formation on the left cheek, which is spreading rapidly and is surrounded by a faint zone of erythema.

of epistaxis until the headaches began; since when it had occasionally accompanied the headaches, never being profuse and being always easily stopped. The teeth had been good until the first child was born; they had ached often since, and several had been extracted; a few had been filled. She had pyorrhea; there was no history of sore mouth, nor of diphtheria. Until two years before, she had had recurrent herpes labialis at the angles of the mouth. There was no history of nasal discharge, catarrh or nasal operations. Colds were frequent, with coughing and rhinitis, but she had had none recently. She had had "weak lungs" seven years before, treated at the Johns Hopkins

Hospital. At that time she had hemoptysis, night-sweats and an afternoon rise of temperature, together with loss of weight—from 180 to 129 pounds. She still had night sweats (?). There was no history of heart trouble. Her ankles and legs often became swollen so that she could not lace her shoes nor walk. She slept comfortably on one pillow; there was no dyspnea nor orthopnea. Her heart palpitated and she felt short of breath when she climbed a few stairs. She had had palpitation and shortness of breath for the last seven years. Her appetite had always been good, until she had influenza two years before, since which time it had often been poor. There had been no stomach trouble. She had been constipated frequently. There was no diarrhea, no history of hemorrhoids, nor of urinary trouble and frequency.

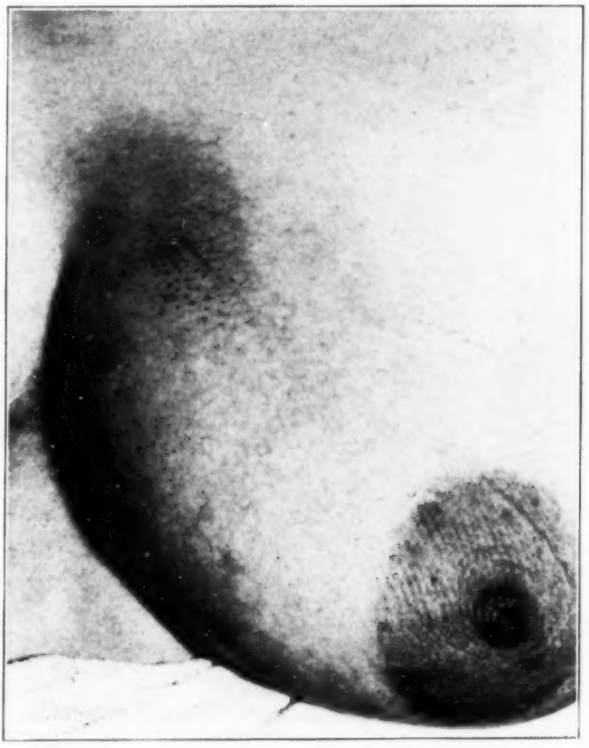

Fig. 2.—Condition on the third day of menstrual period, showing dollar sized area of follicular petechiae on the left breast near the sternum, accompanied by slight erythema. The patch is spreading.

Menstruation began at the age of 12, and the second period occurred six months later. After that, it occurred regularly every twenty-eight days, lasting six or seven days and was quite profuse, associated with cramps which at times were severe. This kept up until her marriage eleven years before, since when she had menstruated every three weeks, and often twice a month, the periods being irregular. There were severe backaches at each period, and cramps the same as before her marriage. There had been a very scanty flow for the last four or five years, lasting four or five days each time, with a white discharge at times between the periods.

There had been no history of joint pains until the last four years, since when she had had occasional pains in the ankles, often so severe that she could not touch the parts. There was no history of any accidents or fractured bones. Seven years before, she had a yellow, weeping, vesicular patch on the skin of the left calf, which appeared independently of her menstrual period.

Present Illness.—One and a half years before, at the time of the menstrual period, she noticed a burning sensation under the left eye. A little red spot, followed by blister formation, appeared, later becoming covered with a yellow crust. The same phenomenon had accompanied each menstrual period since then. The patch had increased in size each time, until it now occupied the entire left cheek and part of the left side of the nose. Four months before

Fig. 3.—Patient on fifth day of the menstrual period, showing involvement of the entire cheek; erythema, edema, follicular hemorrhages and blood crusts, with remnants of small vesicles. The patch resembles an ordinary recent bruise.

she first noticed a similar spot over the skin of the lower sternum; this likewise appeared with each period and at no other time, and increased in size each time, until it extended over part of the left breast including its lower quadrant. During the period of gestation, in the winter of 1919, there was an entire absence of the eruption. The burning sensation preceded the appearance of all the efflorescences.

Physical Examination.—The patient was a well developed, well nourished, somewhat adipose woman of 30 years, able to be about daily, and apparently in good spirits. She was fairly intelligent, and cooperated fairly well with the examiner. The skin was of good color, of normal moisture and texture,

with a rather liberal supply of subcutaneous fat. On the abdomen were multiple lineae albicantes. In the left hypochondrium appeared a flat, depressed soft, pitted, depigmented scar, as large as a 50 cent piece, the origin of which was unknown.

The lesions which directly concern us occupied the left cheek and the midsternal region, with an extension involving the left breast. They appeared as diffuse, brownish-red patches, irregular in size and outline, with a few remnants of brown crusts; the follicles in these areas appeared as darkbrown punctae.

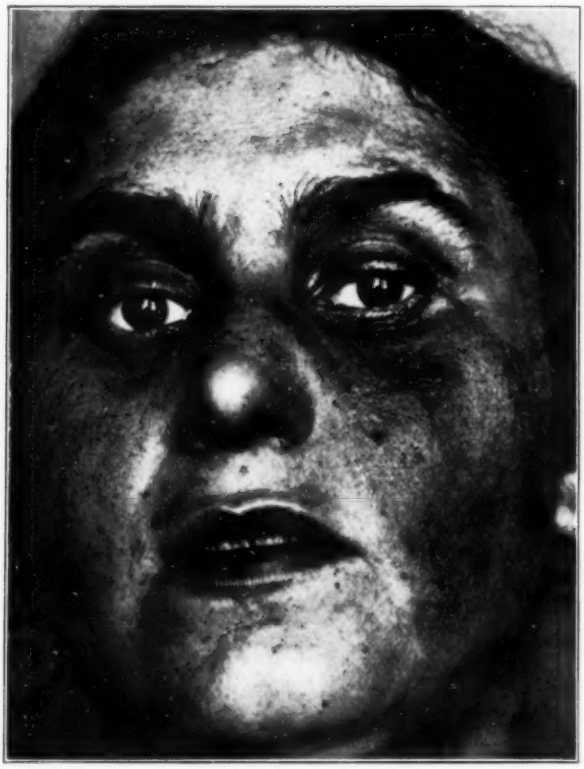

Fig. 4.—Patient on eighth day of menstrual period, showing the lesion on the left cheek in the final stages of evolution. The left cheek is somewhat edematous, yellowish and shows scattered, small adherent blood crusts located in the follicular orifices.

The corneal and pharyngeal reflexes were active. The thyroid gland was normal in size and shape. Examination of the heart and circulatory system proved negative; but auscultation in the second intercostal space, just to the right of the sternum, revealed a slightly tympanitic quality in the note of the second (aortic) sound; this was not transmitted elsewhere. Abdominal visceral examination was negative

There was a little superficial hyperesthesia on the anterior surface of the left leg and thigh; there was no disturbance of temperature sense in this

area. There were varicose veins. No edema or cyanosis was present. The reflexes were normal throughout. The gynecologic examination made by Dr. Combes, Jr., proved negative, with the exception of the presence of a slight cervical tear.

Blood count, June 16, 1920, revealed: white blood cells, 11,400; red blood cells, 4,476 000; hemoglobin, 75 per cent.; polymorphonuclear leukocytes, 68 per cent.; small mononuclears, 24 per cent., and large mononuclears, 8 per cent.

Urine examination revealed: acid reaction; specific gravity, 1.013; no albumin, sugar or casts.

The blood Wassermann reaction was negative. A spinal puncture was not made.

Unfortunately, the patient refused to submit to a biopsy.

Neurologic Examination.—We are indebted to Dr. Louis Casamajor for these reports:

"NEUROLOGICAL DEPARTMENT, COLLEGE OF PHYSICIANS AND SURGEONS

"May 24, 1920

"In connection with the above case, referred to us today, examination shows no evidence of any organic nervous disease. The question of the presence of a psychoneurosis must be held open. She shows some slight signs of an anxiety type of neurosis which may be due to her skin lesion in part. I do not think it is causative."

"June 4, 1920

"I have just examined your patient, Mrs. M. B., and feel that I have little to add to the diagnosis. Besides the facial rash on the left side which she has had for the past eighteen months, for the past two months she has been complaining of a pain and weakness in the left arm and leg of an obvious neurotic character. Physical examination is quite negative, except for a general deep tenderness with superficial hypo-esthesia confined to the left side of the body, which is a typical neurotic finding.

"It is rather difficult to learn much of this person's personality. She is a dull, stolid, not to say stupid, individual, and one whose personal history it is difficult to obtain. She appears to be fairly well satisfied with her life, probably a little more so than most people. She has been married for eleven years and has borne three children, of whom two survived. She seems fairly satisfied with her husband, except for the fact that his earning capacity is low. She apparently is not a deep feeling person, with little desires of any sort, but what she has of love desires seems to be satisfied by her husband with but little effort on his part. I do not feel that there is anything psychogenic in this rash. The type of neurosis from which she suffers is a superficial one and probably has much more to do with her maladjustment in her social and financial sphere, than to anything more deeply instinctive."

Subsequent Observations.—The patient visited us for the first time, April 29, 1920, within a day or two after the termination of the menstrual period. The lesions at that time had almost completely involuted, so that nothing more than a brownish yellow patch of pigmentation was seen on the left cheek and left breast. As stated, she lived in Maine, and was then on the point of going back to her home; but the desirability of remaining here until the next menstrual period

was explained to her, to enable us to observe the eruption in its earliest stages and subsequent development. To this she agreed. Thus we were enabled to note the various cyclical changes pictured in the affected areas, from the beginning to the end of two successive menstrual periods.

At her initial visit, she complained of severe pelvic "cramps." Twenty drops of benzyl benzoate, to be taken twice daily, was prescribed, to be administered as soon as the first signs of menstruation became manifest. The remedy proved efficacious in preventing the onset of the usual cramps but the eruption appeared exactly as it had before and at the same relative time.

DESCRIPTION OF THE ERUPTION

The eruption is best described by enumerating its successive stages: (1) burning or tingling, (2) erythema, (3) edema, (4) vesiculation, (5) exudation, (6) hemorrhage, (7) crust formation and (8) pigmentation.

Two or three days before the beginning of the menstrual period, the patient experienced a burning or tingling sensation in various parts of the body, most frequently on the cheeks and breasts. As soon as the menstrual flow was established, a faint red spot appeared on the left cheek, near the nose, and on the left breast, near the sternum. The opposite areas, on the right side, remained unaffected as to the eruption, but the subjective sensation continued, gradually subsiding with the progress of the menstrual cycle. In the two affected sites, the areas of erythema became slightly elevated and assumed the appearance of an ordinary urticarial wheal. This lasted from six to eight hours. Soon thereafter, the surface of the patch took on a stippled appearance—due to the prominence of the dilated follicular orifices. Up to this stage, both the facial and mammary patches underwent identical changes. Then a divergence took place. The process in the facial lesion went on to the formation of distinct, pinhead sized vesicles, filled with clear serum. These vesicles, which lasted about one day, were perifollicular in location, and, soon bursting, their remnants coalesced to form a uniform patch of what looked like an ordinary weeping dermatitis. This lasted two or three days and was followed by quite distinct, although very minute hemorrhages into the follicle mouths. The appearance then was that of an existing dermatitis which had been severely bruised subsequently, causing slight superficial hemorrhages; it looked much like the injury one sustains by falling on the pavement and scraping the skin of the face against the stones. Almost as soon as the hemorrhagic stage was reached, involution began; the lesion became crusted; the crust adhered for three or

four days and gradually dropped off, leaving a somewhat reddened, edematous and pigmented area, very much like that following an ordinary bruise. This area was surrounded by a broad band of erythema.

In the breast lesion, the process seems to come to a standstill as soon as the follicular hemorrhages supervene. The final stage here (at least on the two occasions when we observed the spots on the breast) appeared to be a circumscribed area of slightly inflamed, yellowish skin, in which the follicular orifices were filled with tiny brownish plugs of dried blood (Fig. 2). This area also was surrounded by a faintly erythematous zone. Finally, resolution took place, leaving a faint, yellow pigmented spot with indistinct borders.

The duration of the active eruption varied from a week to ten days.

It is to be emphasized that at the very inception of the patches the epidermis was intact.

COMMENT

The eruption corresponds in all essential features to that described by Matzenauer and Polland. The progressive cyclical changes, beginning with burning and tingling and ending with follicular blood crusts and pigmentation, are identical. The points of divergence are the absence of symmetry and the absence of necrotic and linear lesions in our patient. Both these are unessential features, however, for the confirmation of the diagnosis of dermatitis dysmenorrheica. Some of Matzenauer and Polland's patients had eruptions which were at times unilateral, and not all of their patients had linear necrotic lesions.

Since our patient was in good health, and refused to stay in a hospital, we were unable to follow the usual procedures of stable and impervious bandaging, strict surveillance, etc., to eliminate the possibility of malingering, or the question of conscious or unconscious self-infliction. We can only state our belief, not to say conviction, grounded at least in part on experiences with true malingerers, that the lesions in this patient were entirely spontaneous.

Perhaps it is not amiss to add that the eminent neurologist who examined the patient on two occasions received the same impression.

The fact that there was an entire absence of the eruptive phenomena during her pregnancy in the winter of 1919 is worthy of reiteration.

In addition to the benzyl benzoate prescribed for the dysmenorrhea, the patient was ordered to take a preparation of endocrine extracts. To the lesion on the face, one unit (skin distance) of roentgen rays was applied, in four divided doses, at weekly intervals. Subsequently to this treatment, she returned to Maine. At the time of the next

menstrual period she reported by mail that there was no recurrence of the face lesion, but that the patch on the breast (which had not been radiated) was "very bad." This vague report has not, however, been verified as yet. We venture the opinion that until a more definite account of the subsequent behavior of the eruption is obtained, the question of the effect of the radiation is not to be seriously considered. Whether or not the endocrine extracts, empirically prescribed, had any beneficial effects in a month's time, is also a matter for speculation.

FURTHER REPORTS IN THE LITERATURE

The occurrence of cutaneous eruptions associated with menstruation is, of course, quite common. In 1906, Bulkley [3] published a booklet on the subject. In this he quotes all the relevant literature up to that time. In relating the case reports in the literature, Bulkley does not attempt any separation between the ordinary "menstrual" eruptions and "dysmenorrheic" eruptions. Some of his quotations of interest in connection with dermatitis dysmenorrheica are as follows:

> Edebohls [4] has reported the case of a girl, aged 19, who presented a peculiar erythematous eruption on the right side of the face, from the middle of the temple to near the angle of the jaw. The eruption had appeared regularly two days before the menstrual flow, fading with its cessation. This had occurred for three years, from 15 to 18 years of age, with then an interruption of nine months, when it again recurred regularly each month. She suffered from severe dysmenorrhea, for which she was curetted, when the eruption ceased for three months. Double ovarian disease was then discovered, and the organs were removed, but the eruption "reappeared with clock-like regularity once a month," and rather more intensely.
>
> Laredde [5] presented at the French Dermatological Society a woman, aged 33, who for nearly twenty years had had certain eruptions recurrent at almost every menstrual period. On the face the eruption was herpetic, but on the hands there were papules and patches of erythema multiforme, and on the legs occasional purpuric lesions. (Dysmenorrhea is not mentioned.)
>
> McGillicuddy [6] records the case of a young lady, aged 20, with extremely painful menstruation, who had, with each period, swelling of the left foot and leg, and also of the face. He says, "I have seen her face much distorted on these occasions by edema around the eyes and at the base of the nose."
>
> Engelmann [7] mentions two cases in which there were small tumefactions on the forehead, breast and back, which appeared at the time of menstrual con-

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3. Bulkley, L. D.: Influence of Menstrual Function on Certain Diseases of the Skin, New York, Rebman Company, 1906.

4. Edebohls, G. M.: New York J. Gynec. & Obstet. **2**:55, 1892; ibid. **3**:48, 1893.

5. Laredde: Ann. de dermat. et syph., 1899, p. 130.

6. McGillicuddy, T. J.: Functional Disorders of the Nervous System in Women, New York, William Wood & Co., 1898, p. 77.

7. Engelmann: The Hystero-Neuroses, Tr. Am. Gynec. Soc., 1887.

gestion, passing away with the cessation of the menstrual flow as rapidly as they had come. The patients were the subjects of uterine disease and suffered from many other reflex symptoms.

Bulkley further quotes numerous examples of menstrual eruptions, such as herpes, urticaria, angioneurotic edema and erythema multiforme, occurring in women whose menses were normal, as well as in those afflicted with dysmenorrhea and other pelvic disturbances.

None of the cases in Bulkley's booklet, however, falls into the same category as our case of dermatitis dysmenorrheica. His cases are all banal skin diseases, occurring at the time of the periods, or aggravated by the onset of menstruation.

In the *Ikonographia dermatologica* for 1909, Zieler published an interesting article entitled, "Exanthema menstruale angioneuroticum." In the case reported by him, there were also no symptoms of dysmenorrhea, but the eruption had appeared, for three and a half years, just before each menstrual period, and had vanished between the periods. The parts affected were the ears, the backs of the arms and hands, especially the fingers, the gluteal region, the sides of the legs and the backs of the feet. The eruption was of the "angioneurotic edema" type, with urticarial wheals and inflammatory nodules, associated with petechiae.

In the last two or three years, several articles on dermatitis dysmenorrheica have been published by Brauer and by Polland. Unfortunately, these are not available at present, with the exception of a brief article by Brauer. In 1917, Polland [8] published a second article entitled "Dermatitis dysmenorrheica symmetrica," and in 1919,[9] an article on "new clinical studies to clarify the differences between dermatitis dysmenorrheica, herpes neuroticus and self-inflicted dermatoses." Brauer,[10] in 1918, published an article under the presumably satirical title, "A Case of So-called Dermatitis Symmetrica Dysmenorrheica in the Male." Whereupon Polland promptly took pen in hand, attacking and criticizing Brauer's conceptions and opinions on the subject, thus rousing Brauer's ire to the point of publishing a brief but cogent reply. In this communication, Brauer [11] maintains his view that the syndrome described as an entity by Polland may be demonstrated in the male

8. Polland, R.: Dermatitis Symmetrica Dysmenorrheica, Arch. f. Dermat. u. Syph. **124**: (April) 1917.

9. Polland, R.: Neue klinische Beiträge zur Klarstellung des Unterschiedes zwischen Dermatitis dysmenorrheica, Herpes neuroticus und Selbstschädigung, Dermat. Ztschr. **28**: 1919.

10. Brauer, A.: Dermat. Ztschr. **26**: 1918.

11. Brauer, A.: Nochmals ein Fall sogenannter Dermatitis symmetrica beim Manne, Dermat. Ztschr. **29**:211 (April) 1920.

sex. He fortifies this opinion by quoting Edel,[12] who, under the title "Multiple Psychogenic Skin Defects of Inflammatory Character," described a case of dermatitis "dysmenorrheica" in a 13 year old boy. In this case it was demonstrated that "the inflammatory plaques could arise only on the basis of neurogenous manifestations."

SUMMARY AND CONCLUSIONS

Our patient presents a syndrome which corresponds in all essential details to that described by Matzenauer and Polland. She has dysmenorrhea, and each menstrual period is accompanied by a regularly recurrent, more or less characteristic eruption, manifested by edema, erythema, follicular hemorrhage, crusting, and pigmentation. The patient has a decidedly phlegmatic temperament.

Between the menstrual periods, the eruption vanishes.

During pregnancy the eruption remains in abeyance.[13]

Self-infliction, malingering, neurotic excoriations, etc., play no part whatever in the causation of the dermatosis.

The dermatosis, undoubtedly one of extreme rarity, is in all probability a disease entity.

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12. Edel, K., quoted by Brauer: Nederlandsch. Tijdschr. v. Geneesk. **1**:1433 (May 25) 1918; abstr. Deutsch. med. Wchnschr., 1918, No. 28.

13. Since this was written, we have been informed that the patient has been pregnant three months. During this period there have been seen no signs of the eruption.

VARIOLIFORM ATROPHIC FOLLICULITIS

FOLLICULITIS ATROPHICANS VARIOLIFORMIS

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In May, 1918, Heidingsfeld [1] reported a case of "atrophia maculoso varioliformis cutis." In the following number of the journal MacKee and Parounagian [2] give a complete clinical and histologic record of two cases that they called "folliculitis ulerythematosa reticulata" and, in the course of the survey of the literature of these peculiar and rare conditions, refer to Heidingsfeld's case, while at the same time recognizing its difference to theirs. When I saw these cases I was under the impression that though they differed somewhat clinically, we should establish their identity histologically, for I had had two such cases, the one, identical with Heidingsfeld's, which I [3] exhibited at the Manchester Dermatological Society in 1912 and the other, the facsimilie of MacKee's, which I demonstrated in 1914. Lately I investigated the cases histologically and found that my impression was incorrect. Heidingsfeld, unfortunately, was not able to make a biopsy.

REPORT OF A CASE

History.—The case I now record was that of a young man, aged 17, who in October, 1912, presented himself at my clinic with pitted atrophic scars on both cheeks, more marked however on the left, and beginning on the latter side three-quarters of an inch below the left external canthus extended downward to the angle of the jaw (Figure 1). The scars varied in size from that of a pinhead to that of a split pea and in places two or more had coalesced, forming a furrow. In the lower part some slight capillary dilatation was evident and a few minute comedones could be detected on both cheeks. The condition was first noticed over the left malar region some four years previously, and for two years the patient had gone elsewhere for treatment, but had recently been discharged as incurable, and had been warned that the scarring would extend and eventually destroy his face. The man's hands and feet showed venous stasis with marked hyperhidrosis. Aside from the fact that his mother had been treated at the hospital some years previously for lupus vulgaris, the family history was of little interest.

The patient had not suffered from smallpox nor had had any pustular eruption of the face.

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1. Heidingsfeld: J. Cutan. Dis. **36**:285 (May) 1918.
2. MacKee and Parounagian: J. Cutan. Dis. **36**:339 (June) 1918.
3. Savatard: Brit. J. Derm., (April) 1912, p. 158, and (Jan.) 1918, p. 46.

Fig. 1.—Varioliform atrophic folliculitis. The transverse furrow above was excised for histologic examination.

Fig. 2.—Varus nodulosus; active stage.

I have seen the patient again recently and find the condition practically in statu quo. There has been a slight increase on the right cheek and the pitting seems to be a little more pronounced. There is no evidence of telangiectasis or erythema. Careful palpation gives one the impression that at the edges of the scars the skin, though apparently normal, is slightly firmer than normal, though it does not amount to induration.

Histologic Examination.—I excised the transverse furrow for histologic examination. I found, on examination, flattening of the papillary layer with atrophy of the hair follicles, diminution of elastic tissue and increase of collagen fibers. At the margins of the atrophic area there was perivascular and perifollicular small-celled infiltration. A sweat gland was greatly distended and

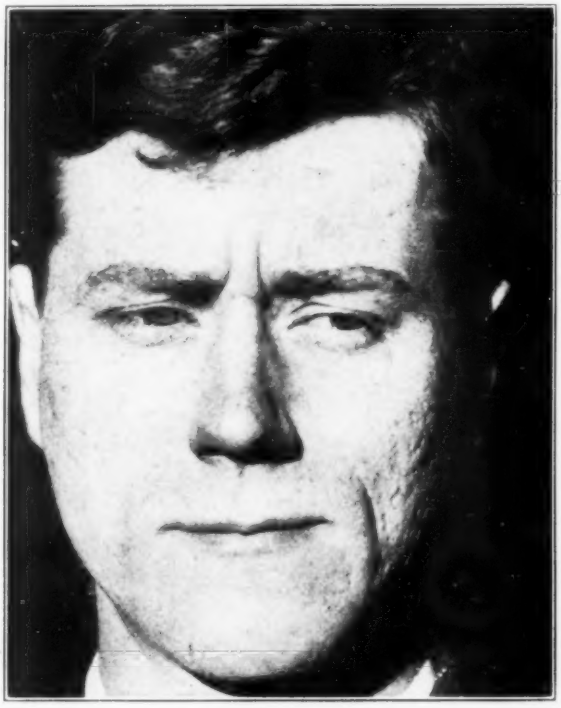

Fig. 3.—Varus nodulosus; atrophic stage.

suggested the obliteration of its duct. There were increased vascularity and proliferation of the vessel walls. The picture was that of an atrophy secondary to chronic inflammation.

I have preferred calling this condition varioliform atrophic folliculitis rather than adopting Heidingsfeld's title. This name not only conveys the clinical picture, but also explains its etiology.

There are, of course, many varioliform atrophic conditions of the skin from which a differential diagnosis must be made; for example, atrophy following follicular lupus, acne varioliformis, and acne agmi-

nata (Radcliffe Crocker [4]), which, however, Brooke [5] described as varus nodulosus. The atrophy in these conditions is, however, secondary to a well marked eruption. Varus nodulosus not only simulates variola in its atrophic stage, but is extremely like it in its initial outbreak, as Figures 2 and 3 show.

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4. Crocker: Diseases of the Skin, Philadelphia, P. Blakiston's Son & Co., Ed. 3, Vol. 2, p. 1096.

5. Brooke: Ikonographia Dermatologica, 1906.

SCLERODERMA AS A POSSIBLE MANIFESTATION OF CHRONIC ARSENIC POISONING*

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In three consecutive cases of diffuse scleroderma seen at the Massachusetts General Hospital within the past six months, the urine has given positive tests for arsenic. One patient, a storekeeper, had kept powdered arsenate of lead under her counter for over four years to kill mice; another had handled glazed paper in a paper box factory for ten years; the third had been exposed to the use of insecticides about the house for a number of years, but so far as could be ascertained, this occurred after the onset of the scleroderma. Further investigation into the records of two other patients, who had died, showed that they had probably been exposed to arsenic. All five of these cases were examples of diffuse scleroderma with brown pigmentation, and the condition of the three patients whom I saw personally and whose urine was positive for arsenic began with sclerodactylia, that being at present the most noticeable and most annoying symptom. Letters were sent to all former patients with undisputed scleroderma of whom we have records, nine in all, but no replies have been received.

Only one case of localized scleroderma or morphea has been studied from this angle. The patient, E. M. (O. P. D. 416812), a young woman in her twenties, had for many years been exposed to arsenic in the form of arsenical sprays in a large garden at home and in her capacity as director of school gardens. Within the past six months there had developed a saber-like, white, depressed firm lesion in the middle of the forehead extending from above the hair line, ending in a point just above the bridge of the nose, and surrounded by pale brown pigmentation. There were no subjective or constitutional symptoms. The urine gave a positive test for arsenic.

Were it not for the fact that scleroderma is such a rare disease, this paper would not be offered for publication until more cases could be analyzed; but it seems desirable to make public the facts so that they may be corroborated or refuted by as many observations as possible. It is not intended here, to urge a connection between scleroderma and arsenic poisoning, but merely to point out the possibility. The original suggestion was offered by Dr. William H. Smith of this hospital in the discussion of Case 1.

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REPORT OF CASES

CASE 1.—*History.*—West Medical 235661. H. E., a man, aged 35, a native of Massachusetts, whose family and past history were unimportant, had been a foreman in a paper box factory for ten years, having come in contact with such materials as glazed paper, cardboard, much paper dust, dextrin, hoof glue and flour paste.

The present illness began one year ago when he noticed that his right hand was weak and that bowling balls slipped out of his fingers. His hands were slightly stiff and the palms a little sore. The soles of his feet were also somewhat sore; he was treated by his local doctor for fallen arches without receiving much relief. After about a month of these mild symptoms he felt comparatively well except for slight soreness of the palms and soles, Six months before entrance into the hospital he noticed that his symptoms were becoming gradually worse. The soreness and stiffness increased; his hands were frequently swollen in the mornings, and they perspired a great deal; at times they were painful on pressure or contact. On exposure to cold the fingers ached and became white or dusky. At present all of his joints are stiff after inactivity, but the fingers are constantly stiff in a position of slight flexion and are capable of little mobility. He had always slept well until about a month ago; since that time he has been restless at night and has slept poorly. He has lost about five pounds during the past year. For the past three months he has taken three pills daily, prescribed by his doctor for "rheumatism." There has been no soreness of the eyes, tongue or throat, and no gastro-intestinal disturbance.

Physical Examination.—This revealed typical sclerodermatous changes with diffuse brown pigmentation involving the hands, forearms, chest and abdomen; the palms were wet with perspiration. The only other positive findings were: a slightly irregular left pupil, enlarged epitrochlear and cervical lymph glands and systolic murmur at the cardiac apex transmitted to the axilla. The blood pressure was systolic 120, diastolic 64. Temperature and respirations were normal. The pulse rate varied between 68 and 85. When seen five months later, there were no changes except for the presence of numerous small keratoses on the backs of both hands.

Laboratory Examination.—The results of the laboratory examination were: urine, no albumin, sugar or sediment on two examinations; renal function, 45 per cent. phenolsulphonephthalein in two hours and ten minutes (normal). The blood smear was normal on two examinations. The white blood count was 8,400; hemoglobin (Talqvist), 80. The routine stool examination was negative. The blood Wassermann reaction was negative. Blood uric acid was 4.1 mg. per 100 c.c. (high). Roentgen-ray examination of the hands and wrists was negative; it showed that the heart was slightly longer than normal. The basal metabolism was 10 (within normal limits). Analyses of the urine and stool for lead and of the stool for arsenic were negative; analysis of the urine for arsenic was positive. Analysis of specimens of four kinds of paper used in the factory, showed arsenic to be present in three—a rough finish gray paper, a tan paper, and a brown cardboard; no arsenic was found in a sample of white glazed paper.

CASE 2.—*History.*—Skin 226621. L. R., a woman, aged 40, born in Russia, lived in Massachusetts for twenty-two years. Her family and past history were unimportant. For the past eight years she has kept a small grocery store

in a damp basement. For over four years it had been her habit to keep an open saucer filled with powdered arsenate of lead under her counter for the purpose of killing mice.

The present illness began about four years ago with numbness, coldness, cyanosis and pallor of the finger tips of both hands. After persisting rather constantly for two years the fingers and hands gradually became stiff and brown. For the past two years there has been a constant aching pain in the hands and fingers, and the stiffness has progressed to practical fixation. During these four years she has been troubled a great deal with pyrosis and eructations without definite relation to meals, relieved somewhat by drinking milk but not by soda; there has been no nausea or vomiting. She never had stomach trouble before her present illness. She has lost 30 pounds in the past two years

Case 2.—Typical sclerodactylia with pigmentation, infiltration and glossy skin. Similar changes involved face and neck. The same condition appeared in Cases 1 and 3. (Photograph by Miss Harriet Williams.)

and feels weak and tired all the time. Recently her catamenia has become slightly irregular and less frequent. Hoarseness has been progressive for many months.

Physical Examination.—This was negative except for typical sclerodermatous changes with diffuse brown pigmentation involving hands, forearms and face. Over both elbows, where the skin seemed firmly attached to underlying structures, a coarse crepitation was heard and felt on motion, a phenomenon not noted elsewhere. Blood pressure was systolic 112, diastolic 70. Temperature, pulse and respiration were normal.

Laboratory Examination.—One routine urine examination was negative. The blood smear was normal. The white count was 14,000 (one estimation), hemoglobin 90 (Talqvist). A Wassermann test and stool examination were not made.

A barium roentgen-ray examination of the gastro-intestinal tract was negative. A urine test for arsenic showed that a considerable amount of arsenic was present.

CASE 3.—*History.*—East Medical 229709. L. R. S., a woman, aged 24, who had always been a resident of Massachusetts, had a negative family history. Her past history showed measles and mumps in childhood, peritonsillar abscess nine years ago which was incised, and pneumonia two years ago. Careful questioning failed to elicit any exposure to arsenic, except possibly through the use of insecticides about the house.

Her present illness began about twelve or thirteen years ago with swelling of the feet and ankles without redness, but with such tenderness that she was forced to give up her work in a shoe factory where she put laces into freshly lined shoes. Some weeks or months later her hands became numb, very brown and so stiff that she was unable to bend her fingers. About five years after the onset areas of brown pigmentation began to appear about the waist, neck, chest and in the joint flexures. About two weeks following pneumonia three years ago she had severe neuritis in both arms lasting several weeks. During the past year or more the numbness and stiffness of the fingers has diminished, and the legs, which several years ago were firm and hard, are now practically normal. She thinks she has lost some weight. She sleeps well. There has been no disturbances of digestion or of menstruation.

Physical Examination.—This revealed marked pyorrhea, bilateral tear of cervix, soft systolic cardiac murmur at apex, smooth and atrophic appearance of tongue on front and sides, dry and scant hair of scalp, axillae and pubes. The skin about the mouth was wrinkled and atrophic, and on the hands and forearms it was glossy, atrophic and firmly bound down. The pigmentation apparently had faded, but was still quite well marked on the hands, forearms, neck, chest, breasts, about the waist and mouth and in the axillae and cubital spaces; on the hands and arms there were areas of depigmentation. The fingers were in partial fixation. Blood pressure was systolic 140, diastolic 80. Temperature and respiration were normal. The pulse varied between 85 and 100.

Laboratory Examination.—Routine urine examination was negative twice except that many white blood cells were present. Renal function was normal with 50 per cent. phenolsulphonephthalein in two hours and ten minutes. Routine stool examination was negative. A Wassermann test was not made. The blood smear was normal; white count 7,000; hemoglobin 80. Blood nonprotein nitrogen was 32 mg. (normal); blood phosphates, 7.8 mg. (normal); blood carbon dioxid 34.5 mm. of mercury (normal). Sugar tolerance test of the blood was normal. Urine test for arsenic was positive. The insecticide in use during the past year was negative for arsenic.

ETIOLOGY

The cause of scleroderma is unknown.[1] A number of investigators[2] believe it is caused by functional or organic disturbances of the glands of internal secretion, especially the thyroid, asserting that a certain degree of improvement followed the feeding of thyroid substance.

1. Stelwagon, H. W.: Diseases of the Skin, Ed. 8, Philadelphia, W. B. Saunders Company.

2. Foerster, O. H.: J. Cutan. Dis. **34**:1, 1916.

Glandular pathology or dysfunction has not been a constant finding, and thyroid therapy has resulted in many disappointments. A basal metabolism of +10 in Case 1, however, does not suggest either a thyroid deficiency or a hyperactivity as we understand it at present. A trophoneurosis is difficult to rule out. Vascular changes in the skin which frequently occur, sometimes progressing to occlusion, are probably secondary rather than causative. A review of the literature during the past twenty years and of all the available textbooks on dermatology has failed to reveal a single statement regarding scleroderma as a possible manifestation of chronic arsenic poisoning.

ARSENIC IN THE URINE

Arsenic may be found in the urine from three to nine months after exposure has ceased. The tests in the cases reported above were made by the Sanger method in the laboratory of Dr. W. Denis of this hospital. The estimations were purely qualitative.

It may be asked how many people, or at least people without arsenic poisoning, will show arsenic in the urine. J. J. Putnam,[3] in 1890, showed that arsenic was present in traces in twenty-one of forty-eight specimens of urine selected from patients in the outpatient department of this hospital who showed no symptoms referable to arsenic poisoning. He concluded from this that the discovery of arsenic in the urine cannot be taken as conclusive proof, or even as strong evidence, taken by itself, as to the origin of doubtful symptoms. On the other hand, "notwithstanding the diagnostic value of a urine analysis in suspected cases, it is not to be forgotten that a failure to find arsenic in this way is not a positive proof that it is not in the body, since, as Taylor and others have shown, arsenic may be excreted only intermittently by the kidneys, and even in acute fatal cases, the urine has been found free."

In this hospital records of chemical tests done on various body fluids and secretions have been kept during the last four and one-half years. Arsenic was recorded as present in twelve out of a total of twenty-five tests of the urine, and in these cases, unlike Putnam's series, the presence of arsenic was suspected as a cause for the symptoms in question.

Using these two series as controls, it is seen that arsenic was found in 43 per cent. of forty-eight specimens of urine selected at random, and in 48 per cent. of 25 specimens suspected of containing arsenic. If arsenic were found in a considerably higher percentage of a large series of specimens of urine from scleroderma patients, we would be justified in suspecting arsenic as an etiologic factor—pro-

3. Putnam, J. J.: Boston M. & S. J. **122**:421, 1890.

vided we could show that the patients had not received arsenical medication in the treatment of their disease. As nearly as could be determined by direct questions and by examination of our records, none of the three patients in the cases reported had received arsenic as treatment for scleroderma, but obviously the possibility of having received it in medicine prior to coming under our observation could not be excluded.

SOURCES OF ARSENIC POISONING

About thirty or forty years ago there was an active interest in arsenic poisoning because of its rather frequent occurrence from the widespread and rather careless use of arsenic in various trades and articles of common use. At that time arsenical wall paper was a common source of danger. Public health legislation has no doubt offered considerable protection, yet the danger has not been entirely removed. The following is a list of articles and industries in which arsenic is or has been used:[4] wall paper (red, orange, brown, gray, green); glazed paper and playing cards; rugs and carpets; printed or woven fabrics for use as garments, draperies, etc.; furs; artificial flowers and leaves; oil paint; lithographer's color printing; Venetian and other blinds; linoleum; japanned goods; book cloth and fancy bindings; tinted walls, bronzing, colored soaps, candy, wafers; children's toys, painted rubber dolls, rocking horses, hollow glass balls, etc.; wax ornaments for Christmas trees; anilin dyes; gloves, stockings, handkerchiefs and other articles colored by anilin; tanning hides or curing furs; smelting lead and copper; shot making; scraping paint off ships; tin plate works; galvanizing trades; electroplating; enameling; manufacture of cut glass; candles; artificial leather; hat linings; soaking of silk cocoons; glucose; beer; medicines, Fowler's solution, etc.; "sheep dip" and other insecticides for spraying gardens[5] or for household use.

One might ask how chronic arsenic poisoning could result from association with wall paper colored with arsenical dyes. B. Gosio[6] and others have shown that at least seven species of molds are capable of producing a highly toxic gas, arsin, from minute amounts of arsenical compounds in their culture mediums. This principle is applied in one of the most delicate tests for arsenic, the biologic test.[7] Penicil-

4. Proc. Med. Soc. London, 1880. Oliver, Thomas: Dangerous Trades, New York, E. P. Dutton & Co., 1902, p. 378.

5. Ayres, Samuel, Jr.: Chronic Arsenic Poisoning on a Farm: Report of a Case, J. A. M. A. **71**:2122 (Dec. 28) 1918.

6. Gosio, B.: Riv. d'ig. e san. pub., 1892, p. 201.

7. Autenreith and Warren: The Detection of Poisons and Powerful Drugs, Philadelphia, P. Blakiston's Son & Co., 1915, p. 235.

lium brevicaule, the most important in this group of molds, has been cultivated from the air. It grows readily on decaying paper, bread crumbs, and other substances.

People vary markedly in their idiosyncrasy to arsenic; some are poisoned readily, others are very resistant. Arsenical preparations vary in their toxicity, arsphenamin in reasonable amounts ordinarily being nontoxic, arsin gas highly poisonous, with many gradations between. According to Putnam,[3] "there is nothing more striking in the clinical history of this matter than the fact that a person who once has been poisoned, or who is naturally susceptible, is sometimes affected by exposures that seem absurdly insignificant."

SYMPTOMS

Although localized scleroderma, morphea, may be symptomless except for the objective appearance, generalized scleroderma, of which the three cases reported are examples, nearly always presents constitutional disturbances of varying type and degree. Sir William Osler [8] describes eight cases, some with severe constitutional symptoms. Herman Goodman [9] reviews sixteen cases from the literature. There is a triad of symptoms which is almost invariably present both in diffuse scleroderma and in chronic arsenic poisoning: (1) neuritic manifestations, numbness, tingling, soreness: (2) pigmentation; (3) changes in the skin itself which, however, vary in the two diseases. The comparative symptomatology of the two diseases is given in the table.

A logical and reasonable question may be raised. If scleroderma is a manifestation of chronic arsenic poisoning, why has it never been described as occurring among arsenic workers, or in persons known to have arsenic poisoning? The following facts may account for a failure to connect the two processes: (1) the extreme rarity of both diseases, especially scleroderma; (2) inadequate history in regard to exposure to arsenic in cases of scleroderma; (3) owing to the fact that the average practitioner knows little or nothing of scleroderma, the disease no doubt is often unrecognized; (4) the possibility that scleroderma may be a specialized manifestation of chronic arsenic poisoning and occur independently of other symptoms, just as tabes dorsalis may occur without any concomitant skin lesions and even without the history of infection, and just as the gastro-intestinal symptoms may be the only evidence of pellagra, or lupus vulgaris the only evidence of tuberculous infection. As a matter of fact, in Osler's Case 8, if the sclerodermatous changes could have been erased and a history of exposure to arsenic substituted, from his description of

8. Osler, W.: J. Cutan. Dis. **16**:51, 1898.

9. Goodman, H.: J. Cutan. Dis. **38**:210, 1918.

COMPARATIVE SYMPTOMATOLOGY OF DIFFUSE SCLERODERMA AND CHRONIC ARSENIC POISONING

Symptoms	Diffuse Scleroderma	Chronic Arsenic Poisoning
Neuritic symptoms	Numbness, tingling, aching, sometimes soreness and severe neuritic pains in involved areas, frequent multiple joint stiffness	Similar symptoms; marked cutaneous hyperesthesia
Pigmentation	Invariable, sooner or later; most marked on sclerodermatous areas; may be diffuse. May be mottled (Osler's Case 8)	Common; diffuse or localized, especially on exposed parts or in folds of joints; frequently mottled
Cutaneous changes	Sometimes erythema and edema early (edema of eyelids, Osler's Case 6); later skin becomes hard, bound down, glossy; sometimes ulceration; roughness of nails, loss of hair, hyperhidrosis of palms and soles; keratoses, author's Case 1	Sometimes erythema, frequently keratosis, diffuse or localized to palms and soles, sometimes with desquamation; sometimes papules, pustules, vesicles, or bullae; frequently edema of eyelids, roughness of nails, loss of hair; hyperhidrosis of palms and soles
Loss of weight	Usually marked	Present
Areas of involvement	Frequently extremities and face.....	Motor and sensory symptoms alike affect principally the distal portions of extremities, rarely extending above elbows and knees; face frequently involved
Gastrointestinal	Sometimes pyrosis, constipation, diarrhea, vomiting, abdominal cramps (Osler's Cases 1, 3 and 8); may be no symptoms	Same symptoms are common
Fever	Not constant; there may be several degrees during active progression of disease or at death	At times slight irregular fever
Onset	Frequently with numbness and tingling of hands and feet; sometimes with stiffness of joints; occasionally with symptoms of Raynaud's disease	Frequently with gastralgia or with numbness or tingling of hands and feet
Vasomotor disturbances	Usually present, especially in fingers; vasomotor paresis in Osler's Case 7	Common
Heart	Occasionally irregular or rapid (Osler's Case 7)	Occasionally irregular
Eyes	Not usually affected.....	Frequent conjunctivitis
Muscular weakness	Frequently present as in our Case 2 and Osler's Case 7	Ususally present
Headache	Not usually complained of.....	Common
Mouth and throat	Disease sometimes begins with an attack of sore throat; occasionally hoarseness is present	Frequent sore tongue and mouth; occasional hoarseness and bronchitis, coryza, cough
Salivation	Not recorded	Frequent; marked thirst
Anemia	Occasional	Occasional
Menstruation	Occasionally irregular	Occasionally irregular
Paralysis	Not recorded; disability from fixation	Occasional
Sudden death	Occasional (Osler's Case 7).....	Not recorded

the case, we should have had a fair picture of chronic arsenic poisoning: weakness, marked loss of weight and appetite, gastro-intestinal disturbances, an intense bronze pigmentation, mottled in character, involving chiefly the face, thorax, abdomen and thighs.

Putnam [10] says that "lead, arsenic, and similar poisons do not always accumulate in the same organ of the body . . . but the position of greater accumulation varies according to the rapidity of absorption (solubility) of the special preparation ingested, the rapidity of elimination and similar factors." At the first opportunity a chemical examination should be made of sclerodermatous tissue at necropsy to determine the presence or absence of arsenic.

Concerning pigmentation in scleroderma, Osler [11] remarks that "there may be the muddy brown discoloration which is common in atrophic areas, or there may be a curious mottled or freckled appearance such as we so often see in the arsenical pigmentation about the abdomen. But the most remarkable instances are those in which the entire skin becomes of a deep brownish black like the most extreme form of Addison's disease." He adds that there are frequently accompanying areas of leukoderma.

PATHOLOGY AND TREATMENT

I shall not go into detail on these subjects, as they are adequately dealt with in numerous textbooks. Dinkler [12] and La Grange [13] have shown that nerve centers, peripheral nerves, heart and large vessels are free from pathologic changes. Unna [14] points out that hypertrophy of preexisting collagenous bundles is the main process, and that whatever vascular occlusion occurs is secondary to this, otherwise "we would see at a certain stage, sclerotic vessels running in normal cutaneous tissue, which we do not;" atrophy of muscles and bones, atrophy or hypertrophy of the thyroid, and atrophy of the suprarenal gland, are some of the rather inconstant necropsy findings.[1]

No successful treatment has been found. In some cases the disease undergoes spontaneous involution, in other cases it becomes arrested, and in others death occurs suddenly or after a prolonged and incapacitating illness. Massage and baking are palliative. Quartz light therapy is a suggestion.

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10. Putnam, J. J.: Boston M. & S. J. **119**:2, 1888.

11. Osler and McCrae: Modern Medicine **4**: 1915.

12. Dinkler: Scleroderma, Heidelberg, 1891.

13. Lagrange: Contribution to the Study of Scleroderma with Arthropathia, Thesis, Paris, 1874.

14. Unna: The Histopathology of the Disease of the Skin, New York, Macmillan Co., 1896, p. 1110.

SUMMARY

1. Three consecutive patients with diffuse scleroderma at the Massachusetts General Hospital showed arsenic in the urine, and two of them gave a history of exposure to arsenic. One patient with morphea frontalis had been exposed to arsenic and showed arsenic in the urine.

2. The possibility of scleroderma being a manifestation of chronic arsenic poisoning cannot be affirmed from the evidence at hand.

3. Careful histories as to the possible exposure to arsenic, a detailed record of general symptomatology and arsenic tests of the urine of a large series of cases of scleroderma would tend to determine whether arsenic plays a rôle in the etiology of scleroderma.

4. Arsenic has been found in traces in 43 per cent. of a series of forty-eight specimens of urine selected at random. It would have to be present in a much higher percentage in urine from sclerodermatous patients to be of any significance.

5. Scleroderma and chronic arsenic poisoning possess many symptoms in common in individual cases, such as neuritic manifestations, pigmentation, cutaneous alterations of various kinds, loss of weight with muscular weakness, intermittent irregular fever, gastro-intestinal disturbances, vasomotor instability, rapid and irregular heart, menstrual disturbances, etc. On the other hand, many of these symptoms may be lacking in cases of well advanced scleroderma.[15]

I wish to thank Dr. William H. Smith of the West Medical Service, Dr. David L. Edsall of the East Medical Service, and Dr. Harvey P. Towle of the Dermatological Service for reviewing and criticizing this paper. I also wish to thank Dr. William H. Smith and Dr. E. Lawrence Oliver for permission to report Case 1, in which the patient was a private patient.

820 Baker-Detwiler Building.

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15. In addition to the references already given, the following may be of interest:

Brooke, H. G., and Roberts, Leslie: The Action of Aresenic on the Skin as Observed in the Recent Epidemic of Arsenical Beer Poisoning, Brit. J. Derm. **13**:121, 1901.

Obituary

ISADORE DYER, M.D., 1865-1920

Another eminent American dermatologist, Dr. Isadore Dyer, died suddenly early in the morning of October 12. He had suffered from angina pectoris for two years. On October 11, he saw patients as usual during the afternoon, and went home apparently in his usual good spirits. While his death comes as a shock to the entire profession, of which he was a well-known and distinguished member, it is particularly felt by a large circle of friends in various parts of the country who recall with pleasure his genial smile and his cordial greeting.

Isadore Dyer was born in Galveston, Texas, Nov. 2, 1865. He was educated in Virginia, graduating from the Bellevue High School in 1884. He received the degree of Ph.B. from Yale in 1887. He attended the University of Virginia in 1887-1888 and received his M.D. degree from Tulane University in 1889. He was an intern in the New York Skin and Cancer Hospital from 1890 to 1892, and began the practice of medicine in Galveston. He moved to New Orleans in 1892 where he acted as professor of diseases of the skin in the New Orleans Polyclinic from 1893 to 1908. He was associate professor of diseases of the skin of the Tulane University of Louisiana, School of Medicine, from 1905 to 1908, and since 1908 professor of diseases of the skin. In 1907 he became associate dean and since 1908 has acted as dean of the medical school. He was president of the Louisiana State Medical Society, 1902-1903; of the Southern Medical Association, 1910-1911; of the American Dermatological Association, 1912-1913; of the Association of American Medical Colleges, 1915-1916; and he was a member of various social organizations. He was editor of the *New Orleans Medical and Surgical Journal* since 1896, and later editor of the *American Journal of Tropical Diseases and Preventive Medicine.*

He was appointed a first lieutenant in the Medical Reserve Corps in 1908, and served on the Mexican border in 1916. He was promoted to the rank of major when the United States entered the World War, and served on the staff of Surgeon-General Gorgas. After the war he was promoted to colonel in the Medical Reserve Corps.

For many years he was a member of the Council of Medical Education and was recently elected vice president of the American Medical Association for the second time.

He left a wife, Mercedes Percival, and five children.

Few dermatologists have contributed more articles or written on a greater variety of subjects pertaining to this special branch of medicine than did Dr. Dyer during the thirty years of his active work. His study of leprosy in connection with the Louisiana Leper Home made him a recognized authority on the subject, and his addresses on governmental regulation of leprosy, prostitution and other questions of public health, brought him prominently before the laity and gave him a world wide reputation.

G. H. F.

Abstracts from Current Literature

SUR UNE NOUVELLE DERMATOSE D'ORGINE FILARIENNE, OBSERVEE SUR LES CONTINGENTS NOIRS (GALE FILARIENNE) (A NEW DERMATOSIS OF FILARIAL ORIGIN OBSERVED IN THE NEGRO). J. MONTPELLIER and A. LACROIX, Presse méd. **28**:607 (Sept.) 1920.

The authors describe a papulo-pustular pruriginous dermatosis which is encountered among the Africans and is called "gale ecthymateuse." They find that the disease is due to the embryoes of the *Onchocerca volvulus*.

There is at first a diffuse modification of the skin with exaggeration of the lines giving it a shagreen appearance. This "état chagriné" is present on the trunk but is especially marked on the buttocks and the lumbar region where the thickening often constitutes a veritable pachydermia. Besides this, there is also frequently present a sort of unpolished aspect to the skin which the authors call the "état pencé." This is especially marked on the external surfaces of the arms and legs and over the knees. The skin is finely squamous, the normal lines are effaced, and thickened patches are formed which are analogous to old patches of circumscribed neurodermatitis.

Disseminated over these general diffuse changes are the eruptive elements of the disease varying in size from a millet seed to 50 centimes. The smallest of these are flat, smooth, scarcely marked, glistening papules, not so plentiful on the extremities but abundant on the trunk. Some of these papules become capped by a vesicle which rapidly becomes pustular, leaving a small crust. After removal of the crust one finds a small cicatricial excavation of a grayish-salmon tint. The larger lesions are flat and papular and are covered by a grayish-yellow crust underneath which is a small drop of thick greenish-yellow pus. Occasionally some of them from which the crust has been removed by scratching form ulcerations. Later on, after healing has taken place, the crusts become brown or black, very adherent and cover a depigmented, depressed, cicatricial surface. These cicatrices, small or large and more or less umbilicated, are numerous in some cases.

Vesiculation may also arise without a papular base and is most frequently found on the backs of the hands and fingers, resembling scabies.

The disease is essentially pruriginous, and the attacks of itching are often violent at the beginning of an exacerbation of the eruption.

The general condition of the patients may be affected. Lassitude, stiffness, articular pains, slight fever and gastric disturbances, accompanied by a curious depapillation of the lingual mucosa, are observed. There is a marked eosinophilia and an enlargement of the inguinal glands.

There is also present, usually about the costal margin and iliac crests,

There are also present, usually about the costal margin and iliac crests, small hard cysts from the size of a pea to the size of an almond in which are found the male and female adults of the filarial parasite. (This manifestation of the disease has been known for a long time, and the authors only claim credit for discovery of the etiology of the skin changes described above.)

The cutaneous changes described are due to the presence of the embryos, three or four often being found in the same microscopic field. These embryos, which are never found in the blood, apparently come by way of the lymphatics from the glands and the filarial cysts. No satisfactory treatment is known.

KETRON, Baltimore.

ETUDE ANATAMO-EXPERIMENTALE SUR LE BOUTON D'ALEP (AN EXPERIMENTAL AND ANATOMIC STUDY OF THE ALEPPO BUTTON). J. KYRLE and J. REENSTIERNA, Acta Dermato-Venereologica **1**:9, 1920.

Two cases came under the authors' observation, and they conducted a rather extensive laboratory investigation which is described in detail, with an excellent bibliography. Their principal conclusions are:

1. In the completely developed lesions in man, especially in those that are nearly healed, we find very few or no Leishman bodies. The abundance of the parasites in the tissue depends on the age of the process.

2. Paralleling the diminution of the organisms, certain changes take place in the structure of the tissue. At first, when the lesion abounds in parasites, we find the ordinary changes of early inflammation. Then the epithelioid cells gradually appear; during this time the organisms in the tissue are becoming more sparse. Finally it has a typical lupoid structure and therewith the Leishman bodies have been completely eliminated. The divergences we find in the literature on the subject of the abundance of parasites in the lesions and also regarding the histologic structure of the "button," are explained by the difference in age and state of development at the time of examination.

3. As we have established, the "button" is readily transferable from man to apes and also to dogs. If the virus has developed in the animals, it may easily be reinoculated in several generations; we have not been able to ascertain the limit in this regard. As to their passage through the animal body, the Leishman bodies would seem thereby to be enhanced in virulence. This has the effect of shortening more and more the period of incubation of the lesions: in our experience, the lapse of time between inoculation and the development of the nodule is reduced from a few months to a few weeks. The virus cannot become generalized.

4. The histologic changes of the "button" in animals are in perfect accord with those in man. In examining systematically all the age periods of the process in animals, we have been able to draw important conclusions on the subject of the pathology of the "button" in man, its different stages of development, and so on.

5. By virtue of the results of experiments on reinoculation in animals, we venture that, in persons who have recovered from a first attack, there exists a state of hypersensitiveness, analogous to that encountered in other processes, such as syphilis and tuberculosis.

PARKHURST, New York.

LES ICTERES SYPHILITIQUES DE LA PREMIERE ENFANCE (POSSIBLE SYPHILITIC ORIGIN OF JAUNDICE AND OTHER CONDITIONS IN YOUNG CHILDREN). GERMAIN BLECHMANN, Le Nourrisson **8**:145 (May) 1920.

Observing that jaundice seemed to occur more frequently in children who presented signs of syphilis, either latent or in process of evolution, Blechmann suspected there might be some causal connection. The frequency of hepatic lesions in the new-born and in nurslings affected with syphilis, and the fact that the liver of the fetus is, owing to its location, subjected to the immediate influence of maternal toxins, and is, therefore, one of the organs conserving most readily the hereditary imprint, lent weight to the supposition. He does not regard any particular type of jaundice as being especially character-

istic of syphilis, but passes in review the various types occurring in infants with which syphilis could be shown by the presence of spirochetes and by the Wassermann test to be associated, either as an accidental or as an etiologic factor. While the evidence for syphilis as a direct etiologic factor in jaundice was not overwhelming, he thinks it was sufficient to justify us in considering the question open to debate. He also discusses other conditions which he believes point to syphilitic infection, such as early rachitis affecting more particularly the skull (craniotabes), the presence of palpable bilateral epitrochlear glands, the occurrence of adenoids in infants under 3 months of age, enlargement of the spleen (provided the skin reaction with tuberculin is negative), convulsions not referable to any organic disease nor symptomatic of the onset of an acute affection (the younger the infant the stronger the indication), congenital strabismus if convergent, habitual vomiting yielding to mercury lactate, and brain disease following difficult labor. He concludes, therefore, that in the presence of any of the foregoing conditions a careful inquiry should be instituted, including a systematic examination of the blood serum, the urine and the stools, and if there is any corroborating evidence of syphilis he recommends active specific treatment in the form of intravenous injections of arsenic salts, by the jugular or epicranial veins.

H. R. W., Chicago.

ZUR ENTSTEHUNG DER IMPETIGO (CAUSE OF IMPETIGO). ERNST FLEHME, Dermat. Ztschr. **31**:111, 1920.

In fifty-five cases of impetigo contagiosa investigated bacteriologically, streptococci in pure culture or mixed with staphylococci, according to the age of the lesion, were found. In every case, the organism was of the type *Streptococcus longus*. The organisms always showed hemolysis and acid formation on mannite-litmus-agar. The impetigo streptococci were pathogenic for white mice, when large doses of the sediment of bouillon cultures were injected. At the site of injection, a circumscribed purulent lesion was formed. In man, it was possible through superficial inoculation to form typical lesions of impetigo, from which the organism was recovered in pure culture. In 15 per cent. of the skins of normal persons, and in 89 per cent. of persons with impetigo, it was possible to demonstrate streptococci, which could only be differentiated from the impetigo streptococci by a stronger red tint of the mannite-litmus-agar, and weaker hemolysis. The superficial inoculation of pure cultures of streptococci recovered from normal skin likewise produced an impetigo. In addition, scarification of healthy skin, on which streptococci were demonstrable, led to the formation of impetigo.

It seems that the cause of impetigo is the attack on fertile ground of a large dose of impetigo streptococci. The normal skin appears to have a resistance to the organism. The skin of the patient with impetigo has a lessened resistance to the same organism, yet there remains some resistance. One may consider the impetigo streptococcus as a semiparasitic organism, that under certain circumstances and in certain localities, and with a diminished resistance of the skin, leads to the formation of the disease. In addition, during epidemics, there may be an increased virulence of the organism which overcomes the normal resistance of the healthy skin.

GOODMAN, New York.

HERPES MENSTRUALIS. P. G. Rinsema, Acta Dermato-Venereologica **1**:87, 1920.

The case described by Rinsema presented the following points:

1. It was a skin disease which was considered as herpes because grouped vesicles appeared. It could not be called zoster because it recurred, the vesicles being small, and lasting only one week. The localization was always the same (a spot on the inner surface of the right thigh, also a smaller one on the left).

2. No congenital disturbance could be connected with its etiology.

3. The herpes appeared, when the patient was not pregnant, always a few days before the menstrual flow.

4. Twice the herpetic outbreak persisted throughout an entire pregnancy, until shortly after delivery.

The author blames some circulating irritant, which always finds the same vulnerable spot, the site perhaps of a peculiarly susceptible nerve or of anatomically defective capillaries. To find the source of this irritant is the next problem.

The time of highest development of the ovarian corpus luteum coincides probably with that of the herpetic outbreak. But why should the herpes persist throughout the two pregnancies? Simply because the corpus luteum becomes the corpus luteum verum, and in the third or fourth month its constant function is taken over by the newly formed placenta. Pregnancy and menstruation produce accentuation in certain skin diseases, and in this case herpes is no exception. But why did these herpetic attacks cease during the first pregnancy, whereas they were constantly present in the two succeeding ones? The explanation is that the first pregnancy, endocrinologically, differs somewhat from its successors.

Unfortunately, experiments could not be instituted to find whether the administration of corpus luteum or placental extract would bring a herpetic attack.

Local treatment by the roentgen ray was employed, with a filter consisting of leather and 1 mm. of aluminum, and a cure was obtained.

Parkhurst, New York.

UEBER EINEN FALL VON UEBEREMPFINDLICHKEIT GEGEN QUECKSILBER UND SILBERSALVARSAN (CONCERNING A CASE OF HYPERSENSITIVENESS TO MERCURY AND SILVER-SALVARSAN). Otto Mergelsberg, Dermat. Ztschr. **31**:129, 1920.

A young man, aged 19, was treated for a syphilitic infection. Early in the course of the treatment it was demonstrated that he was hypersensitive to mercury, and the treatment was carried on with silver-arsphenamin (doses from 0.15 to 0.25). The Wassermann test was rendered negative after the fifth injection, but the courses were continued. After the ninth injection, there was an erythema of the chest and back, moderate albuminuria, and the blood picture was: polymorphonuclears, 54 per cent.; large lymphocytes, 5 per cent.; small lymphocytes, 13 per cent.; eosinophils, 22 per cent.; transitionals, 4 per cent., and mast cells, 2 per cent. The eruption spread; the mucous membranes were affected; there was diarrhea; and the patient became much emaciated. After six weeks, he had sufficiently improved to return to the dermatologic department, where further injections of silver arsphenamin were instituted.

After the sixth injection (total of 1.2) a recurrence of the earlier symptoms set in. It took about six weeks more to bring the patient to normal. He will not be treated further unless the Wassermann becomes positive again, and in the light of the experiences to date, the drug to be used will in all probability be neo-arsphenamin.

A summary of the reported reactions to silver arsphenamin is added to the report of this case.

(I hope shortly to have the opportunity of reporting some personal observations on the effect of silver-arsphenamin of German manufacture. Earlier reports in the literature have had nothing but praise for the preparation when properly administered.)

GOODMAN, New York.

RE CONTINUOUS TREATMENT OF SYPHILIS INSTEAD OF CHRONIC INTERMITTENT TREATMENT. JOHAN ALMKVIST, Acta Dermato-Venereologica **1**:97, 1920.

A brief review is given of the methods of antisyphilitic treatment since the sixteenth century. With the idea that the virulence of the spirochetes may rally during the intervals of the customary intermittent treatment, the author suggests the following principles for the treatment of more recent syphilis:

1. The treatment should be continuous, not intermittent, and of great intensity.
2. From the start the treatment should be under serologic control. The sooner the Wassermann reaction disappears and remains absent, the more favorable will be the prognosis.
3. The duration of the treatment is therefore to be decided on the basis of the results of the serologic examination.
4. The treatment may last for a few months, or in obstinate cases for years.
5. Neither mercury nor arsphenamin can be employed alone for protracted continuous treatment.
6. A certain risk accompanies the administration of mercury and arsphenamin simultaneously, so that, for a continuous effect to be obtained, periods of mercurial treatment alone should alternate with periods of treatment with arsphenamin alone.
7. However, for abortive treatment in the physically fit, mercury and arsphenamin may at first be administered simultaneously.

At least 2 gm. of arsphenamin should be given during each series (twenty to forty-five days). In the mercury course of about forty days, the soluble salts are used, except for the last two or three injections when gray oil is used to secure a "depot effect." The usual precautions must be taken to avoid a possible Herxheimer reaction. After an apparent cure, the case must be kept under observation for at least two years.

Several cases are related in which this treatment proved successful. However, it is rather troublesome and expensive for the patient, and indeed, says Almkvist, it has not yet had a sufficiently thorough trial to warrant definite conclusions.

PARKHURST, New York.

LA SIFILIDE GASTRICA (GASTRIC SYPHILIS). ALBERTO FURNO, Riv crit. di clin. med. **21**:157, 169 (May 15 and 25) 1920.

Furno states that pain in the epigastrium that is exclusively nocturnal and is associated with anacidity awakens a suspicion of gastric syphilis. Further indications are symptoms of gastric ulcer (hematemesis, melena) in subjects

whose gastric chemism is characterized by anachlorhydria or at least hypacidity, low pepsin values and deficient digestive power; also linitis plastica and hour-glass constriction of the stomach. The presence of normal gastric digestion or of hyperchlorhydria excludes the possibility of gastric syphilis. The therapeutic test is, however, the most certain and the easiest means of establishing a diagnosis. Any persistent gastropathy that is rebellious to treatment, and whose symptomatology is unusual either as regards its clinical course or its peculiar signs, should be subjected to syphilitic treatment. The roentgenologic examination may be useful in the diagnosis of gastric syphilis, but it cannot be regarded as decisive. The gastric disturbances may be due to a pyloric stenosis or to a tumor infiltrating the walls, the antrum or the fundus of the stomach, but not presenting the typical aspect that characterizes syphilis. Hour-glass constriction has come to be recognized as frequently due to a modification of the structure of the stomach due to gummatous infiltration and syphilitic cicatrization, but it is necessary to exclude the possibility of its being due to purely functional change, such as atonia, spasm or extragastric compression. The genesis of any anatomic change must be examined carefully, since peptic ulcer or a neoplasm may easily be the inducing cause.

H. R. W., Chicago.

ON THE TREATMENT OF LUPUS VULGARIS BY THE LIQUID ACID NITRATE OF MERCURY. H. G. Adamson, Brit. M. J. **2**:123 (July 24) 1920.

Adamson has recently employed the liquid acid nitrate of mercury in a large number of cases of lupus vulgaris, and he believes that he has found in this application a remedy of the selective caustic type which far surpasses any other method of treating lupus in its efficacy and in its rapidity of action.

The patients that have been treated by this method in the skin department at St. Bartholomew's Hospital may be arranged in four classes:

1. Single patches of nonulcerated lupus from the size of a shilling to that of half a crown, and which have received no previous treatment.

2. Old cases of lupus which have been treated by other methods, but in which lupus nodules still remain in the scars.

3. Ulcerated lupus, often of large extent and with much surrounding inflammatory infiltration.

4. The common type of lupus of the nose, involving frequently also the nasal septum, the palate, the upper lip, the cheek and sometimes the lacrimal sac and skin over and around, a type very difficult to deal with by Finsen light or by scraping.

The liquid acid nitrate of mercury is applied by means of a small swab of wool, tightly twisted around the ends of a finely pointed pair of forceps. It is painted on the affected areas freely and with firm pressure, for from one to two minutes, taking care to limit the application exactly to the lupus patches, to isolated nodules, or to ulcerated surfaces. No dressing is applied; a crust generally forms which falls in a few days, and leaves the affected area sometimes completely healed, sometimes as a shallow ulcer which heals in a few days.

In cases of ulcerated lupus, the solution is freely painted on the ulcerating surfaces. This causes considerable pain, but can usually be borne. The surface of the ulcer becomes dry, yellowish white, but in a few days much serous exudation gives rise to a thick, heaped-up crust. At the end of a week the

crusts are picked off or bathed off, and there is then an ulceration with purulent surface, which heals in the course of a week or so. The number of applications required in ulcerated lupus depends on the depth of the inflammatory infiltration which often accompanies these ulcerations.

The good results the author has obtained seem to justify a more general use of the acid nitrate of mercury in the treatment of lupus.

OLIVER, Chicago.

INFECTIOUS ECZEMATOID DERMATITIS. RICHARD L. SUTTON, J. A. M. A. **75**:976 (Oct. 9) 1920.

In a series of seventy-four cases selected at random and scattered over a period of two years, Sutton found a record of concurrent urticarial eruptions in nineteen instances (more than 25 per cent.). The antecedent disorders varied greatly. As a rule the anaphylactic manifestation did not appear until after the staphylococcic disorder was well under way. All of the attacks were nonfebrile. As a rule, the earlier lesions were frankly suppurative (of fourteen cases in which cultures were made, *Staphylococcus aureus* was recovered in eleven) and auto-inoculable. In the earlier stages of the disease, Sutton has found that a mild astringent, such as an aqueous solution of aluminum acetate (0.5 per cent.), or even lead and opium lotion (lotio opii et plumbi subacetatis) is more effective than one of the greasy preparations. At the end of forty-eight or seventy-two hours, however, one may profitably begin the use of a weak ammoniated mercury ointment (2 per cent.) together with a bland dusting powder containing a small amount of boric acid. After the tendency to suppuration has been overcome, phenolated zinc oil may be substituted for the mercurial ointment. For the relief of the pruritus which often accompanies the urticarial lesions, calamine lotion, to which liquor carbonis detergens (from 2 to 10 per cent.) has been added affords much relief. If necessary, a small amount of phenol (1 per cent.) or menthol (0.5 per cent.) may be added to the ammoniated mercurial preparation, and the ointment used in conjunction with the lotion. Internally, alkaline preparations, such as sodium acetate and sodium citrate in large doses, combined, if the patient is nervous and irritable, with the sodium bromid, frequently prove helpful. If these two fail, Sutton has found the most serviceable remedy to be a mixed staphylococcus vaccine. The initial dose should be small (from 25,000,000 to 75,000,000), and he usually repeats the injections every third day, gradually increasing the amount each time.

WAUGH, Chicago.

UEBER TERPENTINOLBEHANDLUNG (KLINGMULLER) MIT BESONDERER BERUEKSICHTIGUNG IHRER ANWENDUNG IN DER DERMATOLOGIE (TURPENTINE OIL WITH ESPECIAL REFERENCE TO ITS USE IN DERMATOLOGY). HEINRICH BECHER, Dermat. Wchnschr. **71**:460 and 481 (July) 1920.

This is also an extensive review of the literature dealing with the use of intramuscular injection of the oil of turpentine as a therapeutic agent. It has been mostly used in trichophytosis but to some extent in other diseases of the skin. Eighty-one patients were treated. Excellent results were obtained in buboes, soft chancre, eczema, furunculosis, sweat gland abscesses and mastitis. Good results were obtained in prurigo, pruritis, pyodermia in adults, drug rashes, and some gonorrheal affections. It was an aid to the treatment

of ulcus cruris, trichophytosis. No benefit was obtained in treatment of impetigo contagiosa, pyodermias of children, chronic prostatitis and gonorrheal arthritis.

The dose established toward the end of the series was 1 c.c. of a 10 per cent. mixture of oleum terebinthinae in olive oil. The interval between injections was not stated, but it was apparently about every four days. The author emphasizes that no untoward results are obtained in this method of treatment, if a strictly pure drug is used. The cases of severe general reactions and albuminuria which have been reported, he is inclined with Karo to attribute to impurities in the turpentine oil. To avoid this he recommends the use of a constant preparation such as "terpichin."

The author emphasizes the importance of giving the drug according to the recommendation of Klingmüller; this is directly on to the muscular fascia about one to two finger breadths below the iliac crest in the posterior axillary line. The article is concluded with a consideration of the various theories concerning the method of action of oil of turpentine as a therapeutic agent.

KETRON, Baltimore.

UEBER LUNGENBEFUNDE BEI MYKOSIS FUNGOIDES UND IHRE BEDEUTUNG (CONCERNING THE LUNG FINDINGS IN MYCOSIS FUNGOIDES AND THEIR SIGNIFICANCE). ERICH KUZNITZKY, Arch. f. Dermat. u. Syph. **123**:453, 1916.

The study of the lungs in Boeck's sarcoid has led to the conclusion that no association exists between tuberculosis and sarcoid, but that one should consider a specific, primary general disease of the internal organs with localization in the skin, and with great regularity also in the lungs. It appears to belong to the group of chronic infectious inflammatory granulomas, of which the etiologic factor has not yet been demonstrated.

Three cases of mycosis fungoides have been studied to date with the object of adding mycosis fungoides to the group of infectious granulomas. Unfortunately, the cases represented the three periods of the disease.

Lung changes were not demonstrable clinically, but the roentgen ray demonstrated changes similar to those of Boeck's sarcoid. In two cases the lung changes were marked. There was a shadow over the lung area, the apexes were clear, and there was an accentuation of the bronchial tube shadows. About the hilus, there was some enlargement and increase of the normal shadow. There was no evidence of inflammatory changes. It is difficult to give an analysis of the findings. The von Pirquet test was negative in all three cases. Subcutaneous tuberculin injections in two of the cases resulted in no diagnostic rise in temperature in one case. Apparently, a case of mycosis fungoides can be considered as showing the lung changes mentioned. In addition, the perivascular lymphoid infiltration, the leukopenia, liver and spleen enlargement, and hyperplasia of the lymph glands link Boeck's sarcoid and mycosis fungoides in the group of infectious inflammatory chronic granulomas.

GOODMAN, New York.

UEBER DAS WESEN DER "DYSIDROSIS" (THE SUBJECT OF DYSHIDROSIS). M. OTA, Japan. Ztschr. f. Dermat. u. Urol. **20**:6 (June) 1920.

Two years ago the writer published a paper on the same subject, in which he stated that vesicular and squamous diseases of the hands and feet due to trichophyton infection resemble the lesions described under the heading of

pompholyx. This observation had been previously reported by Marie Kaufmann-Wolff and by Max Schramek. The writer at that time considered all these affections of the hands and feet, with few exceptions, as ringworm affections.

Kamibayashi agreed with the author in certain points, but also believed that a distinct entity existed to which he gave the name of idiopathic pompholyx to avoid confusion with a type of pompholyx due to fungi infection.

There are cases of vesicular dermatoses from which the fungi cannot be isolated. There are also cases in which fungi have been found in the feet but not in the affected hands. Is it probable, then, that in such cases the feet are infected by fungi while the hands are the sites of dyshidrosis? There are also cases in which the clinical signs are those of dyshidrosis without positive findings of fungi and yet the lesions disappear under antiparasitic treatment. Do not these facts lead us to the supposition that the majority of such cases bear a certain relationship to fungi infection?

LEVIN, New York.

ELECTRICAL DANGERS IN X-RAY LABORATORIES. J. S. SHEARER, Am. J. Roentgenol. **7**:432, 1920.

The recent death of Dr. Jaugeas by electrocution in a roentgen-ray laboratory in Paris serves to direct attention to the danger of operating roentgen-ray devices when proper precautions are neglected, or when the idea of safety is based on a misconception of the fundamental facts involved. The article by Dr. Shearer must be read in toto to be appreciated, for it does not lend itself very readily to abstracting. The closing paragraph is worthy of repetition here:

". . . medical colleges may some day come to realize that special training is needed for those who are to utilize such powerful agencies in their profession. It is quite true that there is not time to train all medical practitioners in all topics, but there should be provided opportunity for those who do specialize in radiology to secure adequate training When this is accomplished this practice should be restricted to medical graduates who have, in *addition* to the regular medical course, such special training as is needed to increase both the usefulness of this agent and the safety of all concerned."

GOODMAN, New York.

RUBBER TUBING AS A FACTOR IN REACTION TO THE BLOOD TRANSFUSION. GEORGE J. BUSMAN, J. Lab. & Clin. M. **5**:693 (Aug.) 1920.

The author reports the results of his experiments on blood transfusion with rubber tubing of a certain brand with the following conclusions:

1. The brand of supposedly pure gum rubber tubing, which in preliminary experiments by Stokes and Busman produced a reaction in arsphenamin administration, is apparently also able, when new, to produce a reaction if used in blood transfusion work.

2. The toxic substance is taken up in sufficient amounts to produce a reaction in patients receiving transfusions of citrated blood through 80 cm. of new rubber tubing of 4 mm. internal diameter.

3. Enough of the toxic agent is taken up by 250 c.c. of normal uncitrated blood drawn through as little as 35 cm. of new rubber tubing (internal

diameter, 4 mm.), en route from the vein to the container of citrate solution, to produce distinct reaction when given through an old tube. It is not, therefore, necessary that whole blood be citrated to absorb the toxic principle.

4. The mechanically removable débris from the inside of new sterilized tubing does not produce reactions when given in suspension in distilled water or 0.18 per cent. sodium hydroxid solution.

5. Further experiment confirms the observations previously recorded that the toxic agent can be removed from the new tubing by soaking it in normal sodium hydroxid solution for six hours.

6. It should be specifically stated that no attempt is made to propose rubber tubing as an explanation of all transfusion reactions which present chills, fever, prostration, etc. Tubing is merely proposed as one factor.

WAUGH, Chicago.

EXPERIMENTAL SYPHILIS IN THE RABBIT. IV. CUTANEOUS SYPHILIS. PART 1—AFFECTIONS OF THE SKIN AND APPENDAGES. WADE H. BROWN and LOUISE PEARCE, J. Exper. M. **32**:445 (Oct.) 1920.

Skin lesions were found to be most abundant and varied in generalized syphilis in rabbits, the manifestations being chiefly alopecias, paronychia, onychia and lesions of the skin proper.

Several varieties of alopecia were noted, the first of which produced an appearance similar to moth-eaten alopecia in the human being; the second was an abnormal looseness of the hair in large areas; the third was associated with definite skin lesions. Paronychia and onychia were infrequent.

The skin lesions consisted of granulomas which resembled the primary scrotal lesions: cutaneous infiltrations of two types, a flattened and diffuse process and an elevated circumscribed papule.

Macular erythemas were also noted which resembled the human type, although they were not definitely shown to be of specific orgin.

EXPERIMENTAL SYPHILIS IN THE RABBIT. IV. CUTANEOUS SYPHILIS. PART 2—CLINICAL ASPECTS OF CUTANEOUS SYPHILIS. WADE H. BROWN and LOUISE PEARCE, J. Exper. M. **32**: 473 (Oct.) 1920.

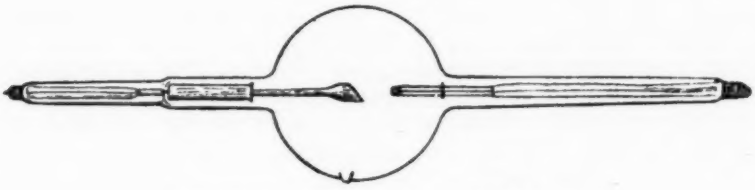
The lesions of the skin manifested in the rabbits studied showed a predilection for certain areas, the character of the lesions differing somewhat in the various locations. The head lesions were mostly small papules or diffuse infiltration; on the forearms and feet they were also of a large granulomatous type, the latter type predominating on the hind feet and legs. It was noted that when multiple lesions appeared in any one area, most of the lesions ceased growing, allowing one or two to reach a considerable size.

The first cutaneous eruption was found to occur approximately from two to four months after inoculation, the earliest being three weeks, the latest two years and eight months. Successive crops of lesions may appear, the duration of lesions varying from a few days in the erythemas to two years in the granulomas. All observations tended to show that the infection had an essentially relapsing course.

JAMIESON, Detroit.

RADIOTHERAPIE PROFUNDA (DEEP ROENTGEN-RAY THERAPY). JOSE GARCIA DONATO and VICENTE GARCIA DONATO, Los Prog. de la Clin. **8**:392, 1920.

A reaction following deep roentgen-ray has been described, the symptoms of which are not unlike those following arsphenamin injections, namely, head-



A Fuerstenau modification of the Coolidge tube.

ache, nausea, diarrhea and other symptoms. Several names have been given, e. g., "Roentgenkater," "Roentgenaterpia," and simple "Roentgen toxemia." The treatment is cessation of the exposures.

GOODMAN, New York.

THE TREATMENT OF SYPHILIS. WALTER J. HIGHMAN, Med. Rec. **98**:477 (Sept.) 1920.

Highman has found the several brands of arsphenamin on the market to be of about equal therapeutic value. He says that any brand which has passed the test of the Hygienic Laboratory in Washington is safe.

The arsenic of an arsphenamin molecule is attached to the spirochete by the benzol ring and brings about a disintegration of the micro-organism. Twenty c.c. of water are used to each decigram of the drug and sodium hydrate is used in excess of the amount needed for clearing the precipitate as a slight overalkalinization is thought to be less toxic.

The author describes in detail the method of injection and suggests the use of a permanent suspension, as supplied by Lowry, for those whose limited experience does not warrant the use of the more difficult method. Mercury salicylate, in conjunction with arsphenamin is used in weekly injections. Intervals of treatment lasting from eight to fifteen weeks are followed by an interval of rest.

The stage of the disease and the results of treatment, as shown by the Wassermann reaction, are used as guides for the amount of treatment needed.

TOMLINSON, Omaha.

LA BOUBA BRASILIANA E UNA LEISHMANIOSI GUARIBILI MEDIANTE IL TARTARO STIBIATO (BRAZILIAN BOUBA IS A LEISHMANIOSIS CURABLE BY TARTAR EMETIC). A. BREDA, Gior. ital. d. mal. ven. **61**:306 (Aug. 12) 1920.

The author, who has been studying the subject since 1895 and has written extensively concerning it, reminds us that kala-azar (produced by Leishmania donovani) and oriental sore (produced by Leishmania tropica) are diseases due to parasites of the same family. He has found similar protozoa in cases of Brazilian boubas and in the diseases known as Baurú ulcer and pian-bois, which Breda asserts ought to be classified together in the same group of diseases due to the leishmanias. In 1913, Vianna of Brazil used for the first

time tartar emetic in the treatment of these diseases. His gratifying results led others to try the new drug, and since then it has been proved without doubt that it is a specific for these diseases. The author reports two cases of extensive and destructive lesions of boubas affecting the extremities, the nose and the mouth, which were entirely cured by intravenous injections of tartar emetic (0.05 gm. in 5 c.c. of sterile water).

PARDO-CASTELLO, Havana.

UEBER EINEN DER PARAKERATOSIS VARIEGATA (UNNA) BZW. PITYRIASIS LICHENOIDES CHRONICA (NEISSER-JULIUSBERG) NAHESTEHENDEN EIGENTUEMLICHEN FALL (A PECULIAR CASE CLASSIFIED AS PARAKERATOSIS VARIEGATA OR PITYRIASIS LICHENOIDES CHRONICA). VIKTOR MUCHA, Arch. f. Dermat. u. Syph. **123**:586, 1916.

A healthy young man, with no hereditary taints, had noticed for fourteen days a generalized eruption of the entire body which gave no subjective symptoms. The erythema was polymorphous, showed macules, slight scaling, papular and papular-necrotic efflorescences, but slightly inflamed, yet decidedly infiltrated, which healed spontaneously, in part without changes in the skin, and in part with scar formation somewhat like that of variola.

The histologic findings in the fresh lesions showed a high grade edema of the upper strata of the cutis and epidermis with a marked epithelial change, massive, extensive perivascular infiltration, especially in the upper layer of the cutis. In the older lesions, the edema was less, but the perivascular infiltration encroached on and ruptured the epidermis. In the central parts were regressive changes in the form of increased cornification and beginning crust formation.

In the differential diagnosis these conditions were considered in the order given: maculopapular or papulonecrotic syphilid; an atypical variola; a tuberculid, and parakeratosis variegata or pityriasis lichenoides chronica, although no mention has ever been made of the presence of necrosis in this affection, and despite the very short course of the disease.

GOODMAN, New York.

VENIPUNCTURE IN THE TREATMENT OF CERTAIN DISEASES OF THE SKIN. JEROME KINGSBURY and PAUL E. BECHET, J. A. M. A. **75**:937 (Oct. 2) 1920.

Kingsbury and Bechet believe that venipuncture is of occasional value in certain asthenic cases of psoriasis, erythema multiforme and dermatitis herpetiformis. It is of great value in the treatment of urticaria, and in their hands affords more relief in severe cases of that disease than any other therapeutic method. They recommend a platinum needle of fairly large caliber (from 16 to 14 gage). The amount of blood withdrawn varies from 100 to 250 c.c., depending on the general condition of the patient. The authors usually bleed the patients once or twice a week. The method is more or less empiric. It has a detoxicating and depurative action on the blood, stimulating the excretory organs, increasing antitoxins, and regenerating the blood mass. In psoriasis, bloodletting seems to be of value in the acute cases with intense congestion around the lesions. The patients were invariably benefited. In erythema multiforme, it is a therapeutic adjuvant of very distinct value. In dermatitis herpetiformis, venipuncture repeated systematically invariably improves the condition of

the eruption and relieves the subjective symptoms. The most gratifying results, however, were obtained in urticaria, particularly in that type of the disease with large raised wheals and associated angioneurotic edema with intense pruritus.

WAUGH, Chicago.

SKIN INVOLVEMENT IN BREAST CANCER, WITH REFERENCE TO ITS BEARING ON THE INTERPRETATION OF APPEARANCES OF TRANSITION BETWEEN NORMAL EPITHELIUM AND CANCER. ALSON R. KILGORE, J. Cancer Res. **5**:291 (July) 1920.

This investigator takes issue with Janeway and Ewing, who express the belief that there is a transformation of normal epithelium into neoplastic tissue, and supports Borrmann, Ribbert and Rous in their contentions that such a transformation is only apparent and that the existing condition is merely a secondary union of the two types of cells due to close approximation. In 475 specimens of breast cancer, seventy-four showed histologic involvement of the skin, but only sixteen showed intimate approximation of cancer to epithelium. Of these, seven showed apparent histologic union but no suggestion of transformation of nonmalignant into malignant cells. In all of these seven cases there was hyperplasia of the normal epithelium, and it was pointed out that the variations in normal cell types associated with hyperplasia lent themselves to the suggestion of transition forms from epithelium to cancer. The morphologic differences between breast cancer cells and skin epithelial cells serve to identify the two types at the point of secondary union.

H. R. FOERSTER, Milwaukee.

SUR LA SYPHILIS CONGENITAL DE LA SECONDE GENERATION (CONGENITAL SYPHILIS OF THE SECOND GENERATION). E. BRUUSGAARD, Acta Dermato-Venereologica **1**:1, 1920.

With the increasing efficiency of antisyphilitic treatment, the disease will more rarely be transmitted to the second generation. In his hospital service the author recently saw a boy of 8 years who presented rhagades about the mouth and serpiginous scarring on the abdomen. The Wassermann reaction was strongly positive. At the age of 1 month, according to the history, there had been an eruption about the mouth, on the extremities and on the abdomen, for which mercurial baths had been given.

The mother, aged 25 years, had had no other children, or any miscarriages. She presented an old bilateral tibial periostitis and the remains of a parenchymatous keratitis which had been active at the time of her confinement. At that time, too, she had suffered from ulcerations of the right leg, and received mercurial inunctions. Her blood gave a strongly positive Wassermann reaction. Furthermore, her history revealed that she had had an eruption involving the face and body when 6 months old, for which she had received mercurial baths. The possibilities of reinfection or superinfection were carefully ruled out.

The maternal grandmother had been infected by her husband; from this infection had resulted a tertiary tibial periostitis accompanied by gummas. Pregnant nine times, she had suffered two miscarriages; three of her children had died in infancy with the signs of congenital syphilis, and another had

died at the age of 8 years with a congenital defect. Of the three survivors, one presented definite syphilitic stigmas and a positive Wassermann reaction, while the second showed neither. The eldest was the mother of Bruusgaard's patient.

PARKHURST, New York.

LA NOUVELLE LOI SUEDOISE SUR LES MALADIES VENERIENNES (THE NEW SWEDISH LAW REGARDING VENEREAL DISEASES). KARL MARCUS, Acta Dermato-Venereologica **1**:62, 1920.

The fundamental principles of the enactment are:

1. An extended service for information and instruction.
2. The obligation of every one contracting a venereal disease to seek the advice of a physician and to conform to his orders.
3. The right of every patient to receive free treatment.
4. The application of certain coercive measures.

The author gives a complete analysis of the various articles. The contagious period is defined, and its vagueness is recognized. If need be, the patient may be placed in a hospital, and here the author advises general adoption of the scheme in vogue at the hospital of St. Göran. Patients with venereal diseases are not placed in a separate ward, but in the general wards side by side with other patients. Thus the stigma usually attached to venereal diseases is largely avoided and, according to the author, the risk of contagion to neighboring patients is nil.

A fund is provided by public taxation to defray the expenses of treatment, both in hospitals and in dispensaries. The patient may choose his own physician, but he is compelled to seek medical advice immediately. Having diagnosed the disease, the physician must notify the patient regarding it and also give information concerning the treatment, prevention of transfer and postponement of marriage until a cure is effected or the contagious period is over. An attempt is also made to ascertain the source of infection in each case. The rules of professional secrecy hold good here as elsewhere, and safeguard the law-abiding patient against any possibility of stigma.

In concluding, Marcus reminds the practitioners that the degree of success of this law will be in direct proportion to the degree of energy and enthusiasm with which they cooperate in its behalf.

PARKHURST, New York.

STATUS OF THE LUETIN TEST. LOUIS HANNAN, Med. Rec. **98**:522 (Sept.) 1920.

Of 100 unselected cases, eleven patients reacted positively to the luetin test. None responded to antisyphilitic treatment.

In checking the influence of medication on the test, mercury and iodids were given for two to three days prior to the application of the luetin, and in thirty consecutive cases the reaction was positive.

Mercury alone was given to ten apparently normal persons, and the luetin tests made following its use were all negative. Some time later six of the ten were tested in a similar way substituting iodid for mercury, and all reacted positively.

The author concludes that the drug reactions are due solely to the iodid, and that the test as now used is unreliable and should be eliminated from standard textbooks.

TOMLINSON, Omaha.

MENINGO-MYELITE SYPHILITIQUE DE LA REGION DORSO-LOMBO-SACREE (SYPHILITIC MENINGOMYELITIS OF THE DORSOLUMBOSACRAL REGION). J. H. LALIBERTE, Bull. méd. de Quebec **20**:321 (July) 1920.

Laliberte's patient, a man, aged 34, who presented a paraplegia of the legs, suffered in addition other motor and sensory disturbances, changes in the tendon reflexes, and disturbances of anal and vesical sphincter reflexes. The history and clinical findings indicated a lesion involving all the cord tissue beneath the tenth and eleventh dorsal vertebrae, involving certain parts more than others, and the meninges as well. The pathologic process consisted of a sclerosis affecting the nerve elements controlling sensation, motion and nutrition of the affected parts.

Tuberculosis, syringomyelia and multiple sclerosis had to be considered in the diagnosis as well as tabes dorsalis; but all of them could be excluded, leaving a diagnosis of syphilitic meningomyelitis of the dorsolumbosacral region. Under antisyphilitic therapy, the patient's condition improved remarkably, and he refused to remain under observation longer.

SENEAR, Chicago

ERYTHEMA BULLOSUM VEGETANS. B. LIPSCHUTZ, Arch. f. Dermat. u. Syph. **123**:523, 1916.

A girl, aged 22, presented on the backs of both hands serous and seropurulent bullae that fitted the well-known picture of erythema bullosum. A unique feature of the case was that previous to the rupture of the bullae, there were formed on their sites smooth elevated, or semispherical buttonlike vegetations. There could be no question of secondary infection, and there was no evidence of systemic disease. In a few weeks, the patient was entirely well. Microscopic and bacteriologic examinations were all negative. The differential diagnosis required finding an affection of papular vegetating efflorescence following bulla formation. Among those known, pemphigus vegetans, dermatitis pseudo-syphilitica vacciniformis, and a disease presenting similar characteristics reported by Reine (later diagnosed mycosis fungoides) were easily distinguished.

The histopathologic findings deserve further study, but from the consideration of description, the condition deserves the application of erythema bullosum vegetans.

GOODMAN, New York.

NUOVO CONTRIBUTO ALLO STUDIO DELLE LESIONI DEL NERVO ACUSTICO NELLA SIFILIDE RECENTE (FURTHER CONTRIBUTION TO THE STUDY OF THE LESIONS OF THE ACOUSTIC NERVE IN EARLY SYPHILIS). J. CAPELLI and C. TORRIGIANI, Gior. ital. d. mal. ven. **61**:243 (Aug. 12) 1920.

The authors report seven cases of acoustic disturbances occurring early in the secondary period of syphilis. All the patients were more or less rapidly affected with sudden deafness of one or both sides, accompanied by dizziness with crisis of vertigo. From the authors' statistics, they conclude that the eighth is the cranial nerve most commonly affected in the secondary stage of syphilis. Acoustic neuritis is frequently accompanied by neuritis of the facial and of the oculomotor nerves. The majority of the patients improve rapidly under specific therapy, but return to normal very seldom occurs.

PARDO-CASTELLO, Havana.

A SERUM AGAINST SOFT CHANCRE, ESPECIALLY ITS BUBOES. JOHN REENSTIERNA, Acta Dermato-Venereologica **1**:146, 1920.

Dead and living streptobacilli were intravenously injected into rams, and the resultant serum was found to agglutinate Ducrey bacilli. This serum has been proved effective therapeutically, and its activity is further enhanced by the addition of a certain quality of dead "feverizing" bacteria (e. g. the typhus bacillus). Previously obstinate lesions have healed rapidly under this treatment, aided, of course, by the usual local therapy. The period of treatment of the buboes, which previously according to many statisticians had been a month or more, has been brought down to somewhat more than one week.

The inconveniences of this treatment are chills and fever after the injection, considerable tenderness for several days at the seat of injection, and sometimes a passing tenderness in regionary lymph nodes.

PARKHURST, New York.

UEBER EINE EIGENARTIGE VERFAERBUNG DER HAUT UEBER DEN VENEN DER VORDERARME NACH ANWENDUNG VON CHYSAROBIN (A PECULIAR DISCOLORATION OVER THE VEINS OF THE FOREARM AFTER THE USE OF CHRYSAROBIN). H. FISCHER, Dermat. Wchnschr. **71**:582 (Aug.) 1920.

In the case reported the patient had been using a 1 per cent. chrysarobin paste and had taken Fowler's solution internally. He had the usual pigmentation about the psoriasis lesions over the body, but over the veins of the forearm the discoloration was much intensified forming dark lines running up and down the arms. This must have been caused by a greater oxidation of the chrysarobin over the veins, but no definite reason for this could be ascertained, although some theoretical possibilities were considered.

KETRON, Baltimore.

UEBER EINE BEZIEHUNG DER GRIPPE ZUR LUES (RELATION OF INFLUENZA AND SYPHILIS). PAULS NEUDA, Wien. klin. Wchnschr. **33**:796, 1920.

Analysis of the case histories of influenza among syphilitic patients gives the impression that the disease runs a lighter course than among non-syphilitic patients. The syphilitic infection is also apparently altered, as shown by the change of the Wassermann reaction toward negative, and an improvement in the findings of the cerebrospinal fluid. The colloidal reaction remains unchanged, however, so that one may not believe that the syphilitic infection is ameliorated, but that the influenza appears to have the power of binding the power of the Wassermann reaction. As other diseases, croupous pneumonia and erysipelas, for example, also have the tendency to alter the Wassermann reaction in syphilitic patients, it would be interesting to observe whether these run a milder course in syphilitic than in nonsyphilitic patients.

GOODMAN, New York.

A CASE OF LEUKEMIA WITH SCALP NODULES. T. H. GUNEWARDENE, Brit. J. Child. Dis. Nos. 193-195:9 (Jan.-March) 1920.

A boy, aged 3½ years, developed more than a dozen pale half inch nodules on the scalp about three months after an attack of measles. The appearance of the nodules was associated with a change in the blood picture from that of

a secondary anemia to that of myeloid leukemia. The nodules increased in number and size and spread to forehead and eyebrows with a decline of the patient's condition, many of them disappearing or decreasing in size just before death. The nodules microscopically showed closely packed aggregations of large mononuclear cells in the muscle layer.

H. R. Foerster, Milwaukee.

EIN BEITRAG ZUR AETIOLOGIE VON VITILIGO VULGARIS MIT BESONDERER BERUECKSICHTIGUNG SEINER BEZIEHUNG ZUR SYPHILIS UND DEN NAEVI (A CONTRIBUTION TO THE ETIOLOGY OF VITILIGO VULGARIS WITH SPECIAL REFERENCE TO SYPHILIS AND NEVI). Shin'ichi Sasamoto, Japan. Ztschr. f. Dermat. u. Urol. **20**:5 (May) 1920.

During the past year the writer studied forty-two cases of vitiligo with special care to determine the relationship of this condition to syphilis. Of the twenty-two patients, who were 20 years of age or older, twelve showed positive signs of syphilis and positive Wassermann tests. In one case there was tabes with the characteristic pupils, reflex signs and lancinating pains. In one case the skin changes disappeared after treatment with arsphenamin and mercury.

In the remaining patients, younger than 20 years, three showed positive signs of erbsyphilis, and in five the Wassermann reaction proved positive. Two of these cases showed positive signs of hereditary syphilis.

Levin, New York.

LA DIFFUSIONE DELLA LEBRA IN SARDEGNA ED IL PRIMO SPERIMENTO DI LOTTA ANTILEBBROSA ESEGUITO IN ITALIA (THE SPREAD OF LEPROSY IN SARDINIA AND THE FIRST ATTEMPT OF AN ANTILEPROSY CAMPAIGN IN ITALY). F. Radaeli, Gior. ital. d. mal. ven. **61**: (Aug. 12) 1920.

The author was a member of a special committee appointed by the Italian government in 1911 to study the problem of leprosy in Italy. In Sardinia, leprosy is widespread. In a small town of 4,000 inhabitants, he found seventeen lepers. Oil of chaulmoogra was used by mouth, as much as 400 drops being given daily. Good results were also obtained with certain proprietaries. Locally, the roentgen ray, ultraviolet rays, carbon dioxid snow and radium were used with advantage in the ulcerative and destructive lesions.

Pardo-Castello, Havana.

UEBER CHLAMYDOZOA-STRONGYLOPLASMEN. IV. UEBER DAS VORKOMMEN VON ZELLEINSCHLUESSEN BEIM IDIOPATHISCHEN HERPES ZOSTER (CHLAMYDOZOA-STRONGYLOPLASMA. IV. CONCERNING THE OCCURRENCE OF CELL INCLUSIONS IN IDIOPATHIC HERPES ZOSTER). B. Lipschutz, Wien. klin. Wchnschr. **33**:836, 1920.

Lipschutz continues his studies and makes his fourth literary contribution concerning the etiology of herpes zoster. He has had the opportunity of studying the skin in cases of zona by modern methods of intravital staining, etc. He is convinced that the "zoster-corpuscles" have some relation to the

disease, and that the reaction formerly described in the nuclei of the cells of the rete is a specific one. Experimental work, already completed and apparently successful, will be reported in a later communication.

GOODMAN, New York.

VENEREAL PROPHYLAXIS IN CIVILIAN LIFE. H. L. SANFORD, J. Urol. **4**:383 (Aug.) 1920.

This article is a plea for the establishment of prophylactic stations for the prevention of disease rather than the indiscriminate use of prophylactic packages by exposed persons. The author believes the station method is much more efficient, although the alternative is better than none.

Estimate is also made of the financial loss in Ohio in one year from venereal diseases. This is stated to be as high as $50,000,000, due to first treatment, loss of time from work, later treatment, complete or partial disability, shortening of life, etc.

He believes in the support of the moral and social agencies now working, and hopes prophylaxis can be added later.

JAMIESON, Detroit.

UEBER NEKROTISIERENDE HAUTHAEMORRHAGIEN BEI HAEMORRHAGISCHEN VARIZELLEN (NECROTIZING SKIN HEMORRHAGES IN HEMORRHAGIC VARICELLA). GUSTAV MORAWETZ. Arch. f. Dermat. u. Syph. **123**:579, 1916.

During the course of hemorrhagic varicella, a boy, aged 3, developed very unusual features as a complication. The ordinary varicella lesions became hemorrhagic, showed evidence of pus formation and led to necrosis, not only at the site of the original varicella lesion, but more extensive, so that large areas were gangrenous. The lesions began to granulate in about four weeks, an accompanying nephritis and bronchitis began to clear up, and the patient was discharged after eight weeks. A colored illustration of the clinical condition accompanies the article.

A MODIFICATION OF HARRISON'S TREATMENT FOR RINGWORM OF THE NAILS. ANDREW L. GLAZE, J. A. M. A. **75**:743 (Sept. 11) 1920.

Harrison advises scraping the nail and then applying on lint, for fifteen minutes, one part of potassium iodid in eight parts of a 50 per cent. solution of potassium hydroxid. Afterward, mercuric chlorid, 1 per cent., in equal amounts of alcohol and water, is kept in contact for twenty-four hours. In most cases it is difficult to scrape away the roughened nail, and the application of the potassium preparation on lint has certain disadvantages. By the method described below, the remedy is confined to the plate and matrix, and the horny tissue is easily removed.

If the fingernails are to be treated, the patient grasps a towel-covered book so that the parts are supported in a horizontal plane. Petrolatum is generously banked about the nails in such fashion that each forms the bottom of a little lake. These are half filled with Harrison's potassium solution, and the softened plate is scraped through the fluid.

The after-treatment with mercuric chlorid sometimes causes severe dermatitis. In its place Glaze has used with safety, and relative satisfaction, a

saturated solution in water of sodium thiosulphate (hyposulphite). It is applied on absorbent cotton, under a rubber fingerstall, six hours or longer, daily for three days.

WAUGH, Chicago.

HEMANGIOMA AND LYMPHANGIOMA; THEIR RESPONSE TO THE INJECTION OF BOILING WATER. FRANCIS REDER, Med. Rec. **98**:519 (Sept.) 1920.

Reder treated 200 cases of hemangioma by injections with boiling water, with uniformly good results. Only five patients became infected and they responded promptly to aseptic treatment. Of eight patients with lymphangioma, two became infected, and although seriously sick, both recovered.

While this method of treatment in lymphangioma is not as encouraging as in angioma, it is considered a valuable asset when intervention seems imperative and operative measures are contraindicated.

TOMLINSON, Omaha.

UEBER DAS STIRNEKZEM INFOLGE HUTLEDERERSATZ UND SEINE URSACHE (ECZEMA OF THE FOREHEAD FROM HAT BANDS, AND ITS CAUSE). GALEWSKY, Dermat. Wchnschr. **70**:353 (June) 1920.

Galewsky reports the frequency in Germany of cases of dermatitis of the forehead due to some irritating substance in hat bands. Due to the scarcity of leather, these bands are made of leather imitations, and the author was able to demonstrate the presence of cresol in them, to which he attributes their irritating quality.

KETRON, Baltimore.

ZUR KENNTNIS DES LICHEN NITIDUS (CONTRIBUTION TO LICHEN NITIDUS). F. LEWANDOWSKY, Arch. f. Dermat. u. Syph. **123**: 494, 1920.

There may still be some relation between lichen nitidus and tuberculosis which has not been suspected. However, to include the affection among the tuberculids is premature. Animal inoculation and the demonstration of the bacillus of Koch (other than in the instance of Arndt) are still lacking. Several clinical characteristics also do not fit the picture of tuberculosis of the skin. Chief among these is the long period in which the affection remains on the same level, without progressing or regressing, which is not noted in any other tuberculid. Localization on the shaft of the penis, a site of predilection of lichen nitidus, is almost unknown for hematogenous tuberculosis. The problem of the specific character of lichen nitidus is not yet answered, but it seems certain that it does not pertain to the group of tuberculids.

GOODMAN, New York.

LINEAR PIGMENTATIONS IN AN ICHTHYOTIC NEGRO. S. MENDES DA COSTA, Acta Dermato-Venereologica **1**:61, 1920.

Apropos of Weidman's article in *The Journal of Cutaneous Diseases*, August, 1919, Da Costa briefly describes a case in which the lines were chiefly transverse and occupied the folds of the skin. The theory is advanced that the pigmentation is due to the penetration of the light into the furrows

where the scales are separated. The horny cells were exempt of nuclei, but contained grains and irregular clusters of black pigment, which failed to give an iron reaction.

PARKHURST, New York.

INTRACISTERN INJECTIONS OF SALVARSANIZED SERUM IN NEUROSYPHILIS. HENRY MCCUSKER, Boston M. & S. J. **183**:490 (Oct. 21) 1920.

The author cites a case of neurosyphilis in which puncture of the cisterna magna was performed between the occiput and the atlas, and he gives the technic for this procedure.

He further suggests that: "(1) Cistern puncture offers another route of application in the method of therapy in syphilis of the central nervous system. (2) It gets the serum nearer to the seat of the disease. (3) It is easier to accomplish than a spinal tap. (4) It offers no more danger than rhachicentesis."

LANE, Boston.

PROTEIN SENSITIZATION IN ECZEMA OF ADULTS. HOWARD FOX and EDGAR FISHER, J. A. M. A. **75**:907 (Oct. 2) 1920.

An interesting report is made of the experimental work done by the authors using Walker's technic. It seems difficult to draw definite conclusions at present regarding the true value of the protein skin tests in eczema of adults. Most of the published reports have dealt with eczema of infants or children. The authors tested each patient by the cutaneous method with a goodly number of the ordinary commercial proteins. The results of these different methods have varied greatly, and they believe that a good deal of investigation remains to be done to determine the real value of the tests. It would appear, however, that they will ultimately prove to be of therapeutic assistance in a small proportion of cases of eczema of adults.

WAUGH, Chicago.

VERAENDERUNGEN DER HAARE UND PILZBEFUNDE IN ZWEI FAELLEN VON CHROMIDROSIS (HAIR CHANGES AND MYCOTIC FINDINGS IN TWO CASES OF CHROMIDROSIS). E. MEIROWSKY, Arch. f. Dermat. u. Syph. **123**:573, 1916.

Two cases of blue chromidrosis were so similar that one description fitted both. The shaft and bulb showed changes indicating mycotic infection. Analysis revealed what seemed to be mycelia, and stained small round bodies, possibly spores. Whether trichomycosis palmellina has an etiologic relation to chromidrosis has not been proved. That a causal relation exists has been often asserted, and the two have been associated in the experience of several dermatologists.

GOODMAN, New York.

MUZINOESE BINDEGEWEBSDEGENERATION IN DER HAUT (FAERBUNG IM PARAFFINSCHNITT) (STAINING OF MUCINOUS DEGENERATION OF THE SKIN IN PARAFFIN SECTIONS). C. KREIBICH, Dermat. Wchnschr. **71**:539 (Aug.) 1920.

The author asserts that beautiful specimens of mucinous degeneration of the skin are obtained by the method which he describes, and also that there is a saving of the reagents used. This method differs from the usual ones in that the paraffin sections are transferred directly, before removal of the

paraffin, into a weak solution of the stain (1 or 2 cm. of stain to 200 or 300 c.c. of warm distilled water). The staining is controlled under the microscope. Afterward the section is transferred to the slide and treated with alcohol, zylol and mounted in balsam.

KETRON, Baltimore.

INVESTIGATIONS RE THE SO-CALLED "MATCH ECZEMA" AND ITS CAUSES. J. STRANDBERG, Acta Dermato-Venereologica **1**:116, 1920.

Considering the number of cases of "match eczema" recently noted, the author undertook a thorough investigation, arriving finally at this conclusion: The so-called "match eczema" is a toxicodermia caused by sesquisulphid of phosphorus which of recent years has entered as the chief component in the striking-surface of certain matchboxes. Probably, bad glue contributes in causing this skin condition. The use of the sesquisulphid has now been discontinued in the match factories of Sweden.

PARKHURST, New York.

SIFILIDE TERZIARIA DELL'ARTICOLAZIONE DELL'ANCA (TERTIARY SYPHILIS OF THE HIP JOINT). L. MORINI, Gior. ital. d. mal. ven. **61**:251 (Aug. 12) 1920.

Morini presents the case of a man, aged 52, who suffered a fracture of the femur two years after a syphilitic infection. A gumma developed at the site of the fracture accompanied by arthritis. Mixed treatment effected a cure although the movements were never normal on account of a hypertrophic callus. This case is interesting because of its rarity, only two other cases having been previously described by Fournier.

PARDO-CASTELLO, Havana.

ZUR FRAGE: GRIPPE UND LUES (CONCERNING INFLUENZA AND SYPHILIS). MAXIMILLAN STRASSBERG, Wien. klin. Wchnschr. **33**:797, 1920.

The Wassermann reaction in the blood and the laboratory findings in the spinal fluid, other than the colloidal gold reaction, are favorably influenced by the fever of influenza. In a series of secondary syphilitic cases, blood Wassermann reactions were reduced to negative, although the influenza had interrupted the therapeutic attack after the first dose of arsphenamin. Other specific fevers are known to have a similar influence. In these facts are found confirmation for the practice of inducing fever in syphilitic patients by the injection of milk and other proteins, which has been done at the Strassbergs clinic.

GOODMAN, New York.

CONTRIBUTO ALLO STUDIO DELLA STRONGYLOPLASMA HOMINIS DI LIPSCHUTZ (CONTRIBUTION TO THE STUDY OF STRONGYLOPLASMA HOMINIS OF LIPSCHUETZ). A. FONTANA, Gior. ital. d. mal. ven. **61**:409 (Aug. 12) 1920.

Fontana refers to Lipschütz' discovery of a parasite in the lesions of molluscum contagiosum. This parasite is a small corpuscle of circular outline, measuring about 0.16 mikrons. It is always present in the lesions of molluscum in isolated form. It stains well by Loeffler's method or by Fontana-Tribondeau's method with silver. This article is illustrated by seven photomicrographs of the strongyloplasma.

PARDO-CASTELLO, Havana.

FREQUENCY OF SYPHILIS WITH CANCER OF THE LIPS, TONGUE AND BUCCAL MUCOUS MEMBRANE. N. Austin Cary, J. A. M. A. **75**:859 (Sept. 25) 1920.

The author's conclusions are based on a study of 907 case histories from the Surgical Pathology Laboratory of the Johns Hopkins Hospital. Syphilis in association with cancer of the tongue is approximately three times more common than in other locations about the mouth—14.5 per cent., or about one in seven cases. This very fact is urgent reason against protracted antisyphilitic treatment in tongue lesions which may be cancer, even in the presence of positive evidence of syphilis. Regardless of the causal relationship of syphilis to cancer, once a neoplasm has been established the prognosis is that of cancer and not of syphilis, and treating the syphilis will not affect the cancer, but will only delay urgently needed surgery.

Waugh, Chicago.

ZUR DIFFERENTIALDIAGNOSE ZWISCHEN MIKROSPORIE UND OBERFLAECHLICHER TRICHOPYTIE DES BEHAARTEN KOPFES (THE DIFFERENTIAL DIAGNOSIS BETWEEN ALOPECIA DUE TO MICROSPORON AND SURFACE TRICHOPHYTOSIS OF THE HAIRY SCALP). Robert Otto Stein, Wien. klin. Wchnschr. **33**:815, 1920.

The conditions under which the children of the various parts of Germany and Austria are living make it very necessary for the physicians to be acquainted with the differential diagnostic points of the parasitic diseases of the hair and scalp. Differentiation is based on three points: (*a*) the clinical picture and course of the disease; (*b*) the microscopic findings of hair examinations, and (*c*) the appearance of cultures.

The efficacy of a concentrated solution of hydrogen peroxid is mentioned, not only for the superficial trichophytosis but for pityriasis versicolor.

TENTATIVI DI RIPRODUZIONI SPERIMENTALE DEL RINOSCLEROMA NELLA SCIMMIA (AN EXPERIMENTAL ATTEMPT TO PRODUCE RHINOSCLEROMA IN APES). A. Pasini, Gior. ital. d. mal. ven. **61**:336 (Aug. 12) 1920.

Two specimens, male and female, of Papio Sphinx were used for these experiments. A fresh culture of Frisch's bacillus was injected in the upper lip, in the nasal sulcus and in the mucosa of the nose of both animals. The results were disappointing. The author reviews the reports of previous attempts of the same nature.

Pardo-Castello, Havana.

UEBER DEN THERAPEUTISCHEN EINFLUSS DER ULTRAVIOLETTEN STRAHLEN AUF DIE DERMATITIS HERPETIFORMIS (THE THERAPEUTIC EFFECT OF THE ULTRAVIOLET RAY ON DERMATITIS HERPETIFORMIS). S. Ehrmann, Arch. f. Dermat. u. Syph. **123**:517, 1916.

Professor Ehrmann, on whose service Lier did his work with the roentgen-ray on Duhring's disease, reports very good results with the use of the ultraviolet ray for the same condition. Indeed, he maintains that the good effects

are more lasting as there was no relapse in a patient who did suffer a relapse following roentgen-ray treatment. This patient was free of symptoms for ten months.

GOODMAN, New York.

CURIETHERAPIE DES RADIODERMITES EPITHELIOMATEUSES PROFESSIONNELLES (RADIUM TREATMENT OF RADIODERMATITIS). DEGRAIS and BELLET, Presse méd. **28**:364 (June) 1920.

The authors emphasize the excellent results which can be obtained in chronic radiodermatitis by radium treatments without the sacrifice of the affected members which is usually advised by the surgeon. They report three cases of professional radiodermatitis which showed keratoses, indolent ulcerations and epitheliomatous formations on the hands. Healing took place under radium treatment and the intense pain also responded to this form of therapy.

KETRON, Baltimore.

SOME VIEWS ON THE TREATMENT OF SYPHILIS CONGENITA. GÖSTA AHMAN, Acta Dermato-Venereologica **1**:109, 1920.

The author agrees with Almkvist in recommending the continuous treatment. The mother should be treated energetically during pregnancy, and the infant should be kept at the breast while its treatment is intensively continued. Salicylate is the preferred mercurial, given intramuscularly. The new salvarsan-sulphaxylate is but slowly oxidizable, and Ahman has found it valuable for intramuscular injection.

PARKHURST, New York.

ZUR PROTEINKOERPERTHERAPIE UNTER BESONDERER BERUECKSICHTIGUN DER SYPHILIS (PROTEIN THERAPY WITH SPECIAL REFERENCE TO SYPHILIS). KARL SCHREINER, Wien. klin. Wchnschr. **33**:748, 1920.

Cases of sycosis vulgaris, lupus vulgaris, scrofuloderma and uncomplicated posterior urethritis (gonorrheal) have been successfully treated with injections of milk, according to the method of Schmidt. Theoretically, there appeared to be indications for the use of milk in syphilis. About twenty patients received injections, but only about half remained under observation. Only one of the ten showed recidive lesions. This case was exceptional in that it did not clear up while the patient was receiving injections. Schreiner reports that lesions of the skin and mucous membranes are favorably affected and that clinically the symptoms disappear after three injections of milk, one given every other day. With arsphenamin he asserts, at least fifteen days elapse before an equivalent result is obtained.

The injections of milk, combined with injections of small doses of neoarsphenamin, have given most excellent results; Wassermann reactions, positive before an injection, have been negative the same afternoon following the injection. The author wishes to collect the data of a larger number of cases observed over a longer period of time before giving definite conclusions.

Similar results without the by-effects of milk have been attained by the intravenous injection of peptone.

GOODMAN, New York.

A FEW CLINICAL OBSERVATIONS ON THE USE OF RADIUM IN MALIGNANT DISEASE. THOMAS H. KELLOCK, Arch. Radiol. & Electroth. **25**:46 (July) 1920.

The writer, after citing cases of rapid early metastases in distant and unconnected parts of the body (abdomen and groins secondary to tongue, rectum secondary to jaw, and other parts) after the local use of radium, infers that such conditions must be embolic or carried by the blood. He advocates the use of radium in a different area, ten or fourteen days before treating the lesion itself, to stimulate a degree of general immunity as a prophylactic measure against metastases. Some other observations by the writer are that the best permanent results seem to follow the use of radium about the periphery of a large growth rather than its insertion into the mass; that radium has more effect in real metastasis than on local recurrences or secondarily infected lymphatic glands; that the action of radium on malignant growths is more marked in cases that are free from septic infection, and that the first application of radium has more effect than any subsequent application.

H. R. FOERSTER, Milwaukee.

TREATMENT OF RINGWORM. W. P. ELFORD, Brit. M. J. **1**:867 (June 26) 1920.

The author reports the cure of sixty cases of tinea tonsurans. The majority of patients were cured within a month's time. He used this method:

The affected area of the scalp is shaved and cleansed with liquid ethereal soap. The part is then gently and carefully rubbed with a piece of lint that has been dipped in potassium hydroxid solution and dried with a piece of absorbent cotton. The part is then sprayed with ethyl chlorid for about thirty seconds, and allowed to dry. It is then painted with diluted tincture of iodin. With the exception of shaving, the remainder of the procedure should be carried out morning and evening for the first three days, and once daily during the subsequent four or five days.

During this time a mild folliculitis occurs, and as a result the infected hairs fall out. Usually a week of such treatment is sufficient to effect a cure, after which it is only necessary to rub ammoniated mercury ointment into the scalp twice daily, keeping the case under observation for two or three weeks.

OLIVER, Chicago.

TREATMENT OF VASCULAR NEVI WITH RADIUM. D. W. MONTGOMERY and G. D. CULVER, Boston M. & S. J. **183**:412 (Sept. 30) 1920.

In this article are reported four cases of vascular nevi of the face and arm. The results obtained are described as extremely good. Treatments were given every three months. The authors caution against treating before complete shrinkage has taken place. A plaque the size of a ten-cent piece, containing 25 mg. of radium, is used. This is screened with 1 mm. of lead, 2 mm. of wood, 12 thicknesses of gauze, and 1 thickness of zinc oxid adhesive plaster to hold them together. The applicator is retained in place for five hours and no burning results from this dose, although sufficient radiation goes through this material to act efficiently on the hyperplastic blood vessels of the tumor. The surrounding tissues must be well shielded with lead, leaving a hole slightly larger than the lesion. In an earlier case radium was screened with

the metal capsules, which had become radioactive from contact with the radium tubes, and a burn had resulted. Under the present technic no burns have resulted, and experience shows that where the skin is not burned by the radium there are no telangiectases.

The flat, red nevus is not nearly so amenable to treatment with radium, but may be much improved. The spider nevus is not amenable to radium treatment.

UEBER DIE WIRKSAMKEIT DES ZUNTZSCHEN HAARWUCHSMITTELS "HUMAGSOLAN" (THE EFFICACY OF ZUNTZ' HAIR FOOD "HUMAGSOLAN"). HERBERT FUHS, Wien. klin. Wchnschr. **33**: 707, 1920.

Fattinger and Company of Berlin have made up a preparation of hydrolyzed horn under the name "Humagsolan." Fuhs has used the preparation in a case of alopecia areata, alopecia symptomatica (following influenza, arsphenamin dermatitis and secondary syphilis), alopecia seborrhoicum (8), and two cases with normal hair growth for control. Fuhs measured the hairgrowth, and the density of hair for weekly and biweekly periods. He is willing to conclude that the preparation is harmless for human beings, but feels that his observations were not numerous or extended enough to indicate its full therapeutic value. Observations on the growth of nails in seventeen patients were not conclusive. There is a normal variation, apparently, in nail growth (about 1.1 to 1.7 mm. for two weeks).

GOODMAN, New York.

UEBER LEUCODERMA NACH DEM SEEBADEN (LEUKODERMA FOLLOWING SEA BATHING). R. TOTSUKA, Japan. Ztschr. f. Dermat. u. Urol. **20**:5 (May) 1920.

The writer is of the opinion that the patches of leukoderma which appear after sea bathing depend on the combined action of sea bathing and sunlight. The lesions are found on the prominent parts of the trunk and on the extensor surfaces of the extremities in the form of a few, discrete, rice seed sized macules. Besides the depigmentation, the affected areas show no abnormality and there is no zone of hyperpigmentation on the periphery of the lesions. The condition appeared two weeks after the baths and in some cases disappeared spontaneously about one year after the onset.

LEVIN, New York.

QUECKSILBERINTOXIKATION NACH INJEKTIONEN VON MERZINOL (MERCURIAL POISONING AFTER INJECTIONS OF MERZINOL). MARIE KAUFMANN-WOLF, Arch. f. Dermat. u. Syph. **123**:433, 1916.

The reports of fatalities following mercury given medically are reviewed, and a case reported of a young woman who succumbed after injections of merzinol given for the treatment of latent syphilis. Although idiosyncrasy may play a part in some of the deaths reported, it is significant that women are more susceptible to this accident than men. Old age, weak constitution, underweight, anemia, nephritis, tuberculosis, myocarditis, alcoholism, poor condition of the gums and chronic angina should be considered as relative contraindications.

Gray oil has been found to be the most dangerous preparation, because the symptoms of its bad effects are not immediately apparent, and the injections are continued until the severe toxic results are introduced.

GOODMAN, New York.

ANTIMONY IN LEPROSY. P. G. CAWSTON, Brit. M. J. **2**:76 (July 17) 1920.

The author reports four cases of leprosy treated with injections of antimony. He used Oppenheimer's colloidal antimony, in doses ranging from 1 to 4 c.c. The injections were administered intramuscularly and were given daily.

He concluded that intramuscular injections had a decided effect on the changes produced in a patient when *B. leprae* is at all active. It seemed to have a beneficial effect on the general condition of leper patients.

OLIVER, Chicago.

UEBER DIE THERAPIE DER DERMATITIS HERPETIFORMIS DUHRING DURCH ROENTGENSTRAHLEN (THE TREATMENT OF DERMATITIS HERPETIFORMIS WITH ROENTGEN RAY). WILHELM LIER, Arch. f. Dermat. u. Syph. **123**:506, 1916.

Three patients who were under observation for a period of several years were resistant to every conventional form of treatment for Duhring's disease. The roentgen ray (dosage, 3 H.) gave immediate relief. At the time of publication of the article, a review of the literature gave but one instance of the roentgen-ray treatment of this affection.

THE PREDOMINANCE OF SEBORRHEIC ECZEMA IN EARLY LIFE. THOMAS S. SOUTHWORTH, Arch. Pediat. **37**:338 (June) 1920.

In the author's experience, the predominating cases of eczema in ordinary pediatric practice are associated with seborrhea. In all such cases he recommends a careful examination of the scalp and the regions about and behind the ears. This type of eczema seemingly has a predilection for fat babies fed on breast milk rich in fat and for bottle babies suffering from disordered digestion caused by a relatively excessive intake of fat.

He believes that a seborrheic tendency forms a suitable medium for the development of dermatitis and mixed infections.

OLIVER, Chicago.

LEUKOPLAKIA OF THE BLADDER AND URETER. HERMAN L. KRETSCHMER, Surg., Gynec. & Obst. **31**:325, 1920.

Kretschmer adds the report of a case to the forty-three already recorded of leukoplakia of the bladder and ureter. Only the opportunity to perform a necropsy on his patient led to the definite finding of leukoplakia of the ureter in addition to the finding of leukoplakia of the bladder. The patient was not syphilitic.

GOODMAN, New York.

THE TREATMENT OF MALIGNANT DISEASE BY ALTERATIVE AND CONSTRUCTIVE MEASURES. WILLIAM BENHAM SNOW, Am. J. Electroth. & Radiol. **38**: (Sept.) 1920.

The writer advocates graded small dosage with continuous tissue saturation as against the single "knock-out" blow in roentgen ray and radium treatment. He proposes radium for superficial growths, roentgen-ray treatment

for deep seated tumors, and the conjoint use of the high frequency current to induce hyperemia in the tumor masses and of desiccation or electrolysis to remove the diseased tissue. In some cases he prefers that the latter methods alone be employed. Thorough roentgen-ray treatment both before and after operation is urged in the management of malignant conditions, such as breast and pelvic diseases.

H. R. FOERSTER, Milwaukee.

UEBER EINEN FALL VON NAEVUS UNILATERALIS COMEDO FOLLICULARIS (REPORT OF A CASE OF NEVUS UNILATERALIS COMEDO FOLLICULARIS). MENAHEM HODARA, Arch. f. Dermat. u. Syph. **123**:409, 1916.

Clinically the case presented large comedones in lines and groups, and brown, small, flat papules and striae. Histologically, in addition to the changes seen in nevus linearis verrucosis, one saw vascular and inflammatory changes of the cutis; acanthosis and hyperkeratosis of the epidermis, and as a special change, the formation of innumerable pseudocomedones. About several of these comedones one found a proliferation of the prickle cell layer and new formation of follicular cylindrical cells which form themselves into small follicles, from the center of which in some cases rises a newly formed hair with complete bulb root.

GOODMAN, New York.

MALIGNANCY OF THE CROWN-GALL AND ITS ANALOGY TO ANIMAL CANCER. ISAAC LEVIN and MICHAEL LEVINE, J. Cancer Res. **5**:243 (July) 1920.

Crown-gall occurs as a benign condition caused by *Bacterium tumefaciens* and is analogous to granuloma or keloid in man, and as a malignant condition not directly caused by the aforesaid bacterium and analogous to animal cancer.

H. R. FOERSTER, Milwaukee.

DIE BESEITIGUNG DES FRAUENBARTES (THE REMOVAL OF THE BEARD OF WOMEN). MAX JOSEPH, Arch. f. Dermat. u. Syph. **123**: 425, 1916.

Joseph gives the following principles for the handling of this type of case:

Electrolysis is to be employed in cases in which the hairs are not too numerous and are thick and bristle-like.

Peroxid of hydrogen or radium is recommended for soft fine hairs.

Roentgen ray or pumice stone are the only two to be considered in full fledged hypertrichosis cases.

GOODMAN, New York.

EIN SELTENER FALL VON ANTIPYRINEXANTHEM (AN UNUSUAL CASE OF ANTIPYRENE EXANTHEMA). HAROLD BOAS, Dermat. Wchnschr. **71**:479 (July) 1920.

The author reports a case of an antipyrene rash in a young girl, consisting of localized areas of edema chiefly on the genitalia.

KETRON, Baltimore.

ZUR KENNTNIS DES WANZENGIFTES (CONTRIBUTION TO THE STUDY OF BEDBUG POISON). E. KLAUSNER, Arch. f. Dermat. u. Syph. **123**:443, 1916.

The secretion of over 50,000 bedbugs was extracted in alcohol, and used in the experiments of Klausner, who says that the active principle of the bedbug secretion is soluble in water and alcohol; that it has an intensive urticarial and hemolytic effect; that free formic acid is not present in the secretion and does not come under consideration as the cause of its effects; and that an immunization against the poisonous effects of the secretion does not seem attainable.

STUDIEN UEBER NUKLEINWIRKUNG (STUDIES ON THE ACTION OF NUCLEIN). PAUL HABETIN, Wien. klin. Wchnschr. **33**:726, 1920.

Habetin has studied the action of sodium nucleinate substituted for ordinary antigens in the Wassermann reaction. Fifty-eight cases were investigated. In thirty-seven there was agreement in inhibition; in eleven cases the Wassermann reaction was positive, and the sodium nucleinate antigen negative; in four cases the reverse occurred; and in six instances both tests were negative. In this series all serums were from known positive syphilitic patients.

Among thirty-eight control examinations, three patients gave positive nuclein tests. Two of these patients had malaria; the third may have been a latent syphilitic with no knowledge of his infection, who temporarily gave a negative Wassermann reaction.

GOODMAN, New York.

A REPORT OF THE WORK CARRIED OUT AT THE RADIUM INSTITUTE DURING 1919. A. E. HAYWARD PINCH, Arch. Radiol. & Electroth. **240**:50 (July) 1920.

This is a report dealing with radium salts and emanation, screening, technic, dosage and exposure, reactions, sequelae and the effects of radium radiation on radium workers, and protective measures for the latter.

H. R. FOERSTER, Milwaukee.

WEITERER BEITRAG ZUR FRAGE DER GOLDSOLREAKTION IM LIQUOR SEKUNDAERSYPHILITSCHER (ADDITIONAL DATA ON THE COLLOIDAL GOLD REACTION OF THE CEREBROSPINAL FLUID IN SECONDARY SYPHILIS). J. KYRLE, R. BRANDT and F. MRAS, Wien. klin. Wchnschr. **33**:745, 1920.

A persistent positive colloidal gold test, even in association with other negative findings is not a favorable prognostic symptom. Rarely has a case been encountered in which the colloidal gold test has been persistently negative and the Wassermann test positive, as the only symptom.

As mentioned in their earlier paper (abstracted in the October issue, p. 513), it is difficult to render the colloidal gold reaction negative even with most intensive treatment, except in those cases in which the change in this reaction is recognized to be only a slight one.

GOODMAN, New York.

TUBERCULOSIS VERRUCOSA CUTIS OF THE FOOT. T. McCRIRICK, Brit. J. Child. Dis. Nos. 193-195:26 (Jan.-March) 1920.

The lesion occurred on the sole of a 12 year old boy. There was active tuberculosis in the family, and it is assumed that the boy, who went barefoot, was inoculated with tuberculosis sputum in a bruise or cut.

H. R. FOERSTER, Milwaukee.

THE OCCURRENCE OF URTICARIA AFTER SPECIFIC FEVERS. E. WARD, Brit. M. J. **2**:278 (Aug. 21) 1920.

The author reports a number of cases of urticaria developing after specific fevers, pneumonia, influenza and other conditions.

OLIVER, Chicago.

UNUSUAL BENIGN EPITHELIAL TUMOR OF THE LID. S. R. GIFFORD, Am. J. Ophth. **3**:602 (Aug.) 1920.

This is a report of a case of a small fibrous nodule, without apparent connection with the overlying epidermis, showing encapsulated nests of epithelial cells with pearl formation and hyaline degeneration.

H. R. FOERSTER, Milwaukee.

TUBERCULOSIS CUTIS VEGETANS. CHRISTIAN VOGEL, Dermat. Wchnschr. **71**:560 (Aug.) 1920.

This is a case report. KETRON, Baltimore.

BASAL CELL EPITHELIOMA OF THE CONJUNCTIVA. DAVID H. COOVER, Am. J. Ophth. **3**:683 (Sept.) 1920.

The author reports the case of a fungoid tumor microscopically diagnosed as prickle cell epithelioma occurring on the site of a papilloma removed eleven years previously. The eyeball was removed.

H. R. FOERSTER, Milwaukee.

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Epithelioma of the Lower Lip. A Clinical Study of. Everett S. Lain, J. A. M. A. **75**:1052 (Oct. 16) 1920.

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